

WEST[Help](#)[Logout](#)[Interrupt](#)[Main Menu](#)[Search Form](#)[Posting Counts](#)[Show S Numbers](#)[Edit S Numbers](#)[Preferences](#)[Cases](#)**Search Results -**

Term	Documents
(1 AND 2).USPT.	2
(L2 AND L1).USPT.	2


US Patents Full-Text Database 

US Pre-Grant Publication Full-Text Database

JPO Abstracts Database

EPO Abstracts Database

Derwent World Patents Index

Database: IBM Technical Disclosure Bulletins **Search:**L3 
[Refine Search](#)[Recall Text](#) [Clear](#)**Search History****DATE:** Monday, September 09, 2002 [Printable Copy](#) [Create Case](#)**Set Name Query**
side by side**Hit Count Set Name**
result set*DB=USPT; PLUR=YES; OP=ADJ*

<u>L3</u>	L2 and l1	2	<u>L3</u>
<u>L2</u>	glucocorticoid receptor	932	<u>L2</u>
<u>L1</u>	gr beta or gr alpha	14	<u>L1</u>

END OF SEARCH HISTORY

*****STN Columbus*****

FILE 'JAPIO'
FILE 'BIOSIS'
FILE 'SCISEARCH'
FILE 'WPIDS'
FILE 'CAPLUS'
FILE 'EMBASE'
=> s glaucoma#

L1 82458 GLAUCOMA#

=> s l1 and glucocorticoid receptor#

L2 68 L1 AND GLUCOCORTICOID
RECEPTOR#

=> s l2 and (glucocorticoid receptor beta or grbeta or
gr-beta)

L3 2 L2 AND (GLUCOCORTICOID
RECEPTOR BETA OR GRBETA OR GR-BETA)

=> s l2 and ocular hypertension

L4 18 L2 AND OCULAR HYPERTENSION

=> s l3 and l4

L5 0 L3 AND L4

=> dup rem l2

PROCESSING COMPLETED FOR L2
L6 40 DUP REM L2 (28 DUPLICATES
REMOVED)

=> dup rem l3

PROCESSING COMPLETED FOR L3
L7 1 DUP REM L3 (1 DUPLICATE
REMOVED)

=> dup rem l4

PROCESSING COMPLETED FOR L4
L8 9 DUP REM L4 (9 DUPLICATES
REMOVED)

=> d ibib abs 17

L7 ANSWER 1 OF 1 WPIDS COPYRIGHT 2000
DERWENT INFORMATION LTD DUPLICATE 1
ACCESSION NUMBER: 1998-333347 [29]
WPIDS
DOC NO CPI: C1998-103395
TITLE Diagnosing ***glaucoma*** and
determining usefulness
of therapeutic agents - by detecting
aberrant expression
of beta ***glucocorticoid***
receptor
DERWENT CLASS: B04 D16
INVENTOR(S): CLARK, A F, WORDINGER,
R J
PATENT ASSIGNEE(S): (CLAR-I) CLARK A F,
(WORD-I) WORDINGER R J
COUNTRY COUNT: 23
PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG
WO 9824932 A1 19980611 (199829)* EN 5
RW: AT BE CH DE DK ES FI FR GB GR IE IT
LU MC NL PT SE
W AU CA JP MX US
AU 9852617 A 19980629 (199845)
EP 943014 A1 19990922 (199943) EN
R AT BE CH DE DK ES FI FR GB GR IE IT LI
LU MC NL PT SE

APPLICATION DETAILS

PATENT NO KIND APPLICATION
DATE

WO 9824932 A1 WO 1997-US21054
19971114
AU 9852617 A AU 1998-52617
19971114
EP 943014 A1 EP 1997-947569
19971114
WO 1997-US21054 19971114

FILING DETAILS:

PATENT NO KIND PATENT NO
AU 9852617 A Based on WO 9824932
EP 943014 A1 Based on WO 9824932

PRIORITY APPLN INFO: US 1996-33227
19961205
AN 1998-333347 [29] WPIDS
AB WO 9824932 A UPAB: 19980722
Diagnosing ***glaucoma*** comprises either:
(i) detecting aberrant ***glucocorticoid***
receptor (***GR***) ***beta*** expression or defects
in a GR gene which
encodes ***GR*** ***beta***
(ii) detecting genetic changes in the GR gene
leading to altered
GR ***beta*** expression, or
(iii) detecting genetic changes outside the GR
gene which lead to
altered ***GR*** ***beta*** expression.
Also claimed is a method for determining
whether an agent is useful
for treating ***glaucoma*** by determining
whether it interacts with
GR ***beta*** or alters the expression
of ***GR***
beta
USE - Cultured human trabecular meshwork cell
lines derived from
glaucomatous donors express mRNA for both on
alternate splice form of the
human ***glucocorticoid*** ***receptor*** (***GR***
beta), as well as the normal
glucocorticoid receptor (GR alpha).
whereas normal tm cell lines only express mRNA
for GR alpha . Determining
that an individual abnormally expresses ***GR***
beta in
their trabecular meshwork or other tissues can lead
to a diagnosis of
glaucoma . Agents that have therapeutic
value for treating
glaucoma can be determined by using
ligand binding assays or
GR ***beta*** functional assays
Dwg 0/0

=> d ibib abs 18 1-9

L8 ANSWER 1 OF 9 WPIDS COPYRIGHT 2000
DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-491060 [43]
WPIDS
DOC NO CPI: C2000-147602
TITLE Diagnosis, prognosis and treatment of
glaucoma
based on detecting specific
polymorphisms in the promoter
of the trabecular meshwork inducible
glucocorticoid ***receptor***
gene.
DERWENT CLASS: B04 D16
INVENTOR(S): CHEN, H; CHEN, P;
NGUYEN, T D, POLANSKY, J R
PATENT ASSIGNEE(S): (REGC) UNIV
CALIFORNIA
COUNTRY COUNT: 89
PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG
WO 2000042220 A1 20000720 (200043)* EN 121
RW: AT BE CH CY DE DK EA ES FI FR GB

GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ TZ UG ZW
W AE AL AM AT AU AZ BA BB BG BR BY
CA CH CN CR CU CZ DE DK DM EE ES
FI GB GD GE GH GM HR HU ID IL IN IS JP
KE KG KP KR KZ LC LK LR LS
LT LU LV MA MD MG MK MN MW MX
NO NZ PL PT RO RU SD SE SG SI SK SL
TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

APPLICATION DETAILS

PATENT NO KIND APPLICATION
DATE
WO 2000042220 A1 WO 2000-US559
20000111

PRIORITY APPLN INFO: US 1999-306828
19990507, US 1999-227881
19990111
AN 2000-491060 [43] WPIDS
AB WO 200042220 A UPAB: 20000907
NOVELTY - A method for the diagnosis, prognosis
and treatment of
glaucoma, based on detecting specific
polymorphisms in the
promoter of the trabecular meshwork inducible
glucocorticoid
receptor gene, is new.
DETAILED DESCRIPTION - Diagnosis, or
prognosis, of ***glaucoma***
comprises incubating a marker nucleic acid (I) that
hybridizes
specifically with a polynucleotide linked to a TIGR
(trabecular meshwork
inducible ***glucocorticoid*** ***receptor***
) promoter with
complementary nucleic acid (II) present in a patient's
cell or body fluid
sample (I) and (II) hybridize and a polymorphism is
detected that is:
(i) predictive of a mutation affecting TIGR
response; and
(ii) diagnostic (prognostic) of ***glaucoma***

INDEPENDENT CLAIMS are also included for
the following:
(a) a similar method for diagnosing sensitivity to
steroids,
(b) a nucleic acid (III) that comprises any of the
sequences (N1)
(5300 bp (base pairs)), (N3) (6169 bp), (N4) (926
bp), (N5) (2099 bp) or
(N24) (1548 bp);
(c) a recombinant DNA (IIIa) that hybridizes
specifically to the
sequences of (b);
(d) a pure molecule (IV) that binds to (III);
(e) a pure molecule (IVa) that binds to any of
about 40 specified
nucleic acids that include a cis-element;
(f) a method for the treatment of
glaucoma by administering
an agent that binds a cis-element present in (N1),
(g) a nucleic acid (IIIb) that is (a region of) (N33)
which comprises
the sequence CAAACAGACTTCCGGAAGGT,
(h) a nucleic acid (IIIc) that hybridizes
specifically to (IIIb),
(i) a vector or cell containing (IIIb),
(j) a method for detecting the characteristic
TIGRmt11 sequence by
hybridization to labeled (IIIb), for detecting
increased susceptibility to
glaucoma, progressive ocular hypertensive
disease or steroid
sensitivity;
(k) a kit for method OF (j) containing labeled
(IIIb) and system for
detecting hybridization.
(l) a nucleic acid (IIId) that is (N1), (N3), (N2)
(5304 bp) or (N34)
(5271 bp) or any of their fragments that contain a
functional regulatory
sequence,
(m) cells or vectors containing (IIId),

(n) a method for detecting the TIGRmt11 sequence variant by amplification,
 (o) kit for method of (n) containing amplification primers and enzyme,
 (p) a method for detecting a polymorphism in the 5'-flanking region of TIGR by amplification with specific primers (sequences reproduced in specification),
 (q) the nucleic acids (N37) (283 bp) and (N38) (227 bp), sequences 95% identical with them or their variants,
 (r) recombinant nucleic acids, vectors and cells containing the sequences of (q),
 (s) identification of a protein or compound that binds to, and modifies expression of, TIGR from ability to bind to (N37), (N38) or their variants, or to regions of (N3) or (N34);
 (t) a method for identifying a compound that modulates the binding reaction in (s); and
 (u) a method for identifying compounds that modulate steroid induction of a TIGR gene.

ACTIVITY - Antiglaucoma, ophthalmic.
 No data given.

MECHANISM OF ACTION - Modulation of expression of the TIGR gene.

USE - The method is used for diagnosis and prognosis of glaucoma (of all types), steroid sensitivity and progressive ocular hypertension that leads to loss of vision. Also glaucoma can be treated by administering an agent that binds to cis-acting elements within the TIGR promoter. The TIGR promoter (or other regulatory regions) can be used to express homologous or heterologous genes, particularly for tissue-specific expression of therapeutic transgenes for treating glaucoma, also to generate transgenic animals and in screening for compounds (specific modulators) with diagnostic or therapeutic potential. Fragments of the TIGR sequence can be used as amplification primers or probes, e.g. for isolating related sequences in non-human animals.

Dwg. 0/9

L8 ANSWER 2 OF 9 MEDLINE
 ACCESSION NUMBER: 2000414284 MEDLINE
 DOCUMENT NUMBER: 20388270
 TITLE: [Hormonal changes in male patients with primary open angle ***glaucoma***].
 Ocena zmian hormonalnych u mezczyzn chorych na jaskrze
 prosta otwartej kata przesaczenia.
 AUTHOR: Nowak M, Swietochowska E,
 Jochan K, Buntner B
 CORPORATE SOURCE: Zakladu Patofizjologii i Endokrynologii Slaskiej AM w Zabrze
 SOURCE: KLINIKA OCZNA, (2000) 102 (2) 103-8
 Journal code: KWC. ISSN: 0023-2157.
 PUB. COUNTRY: Poland
 Journal, Article, (JOURNAL ARTICLE)
 LANGUAGE: Polish
 ENTRY MONTH: 200011
 ENTRY WEEK: 20001101
 AB INTRODUCTION: Primary open angle ***glaucoma*** (POAG) is the most common type of ***glaucoma***, pathogenesis of which is not completely known. Several clinical studies show that glucocorticoid hormones may be implicated in the pathogenesis of POAG and ***ocular***
 hypertension ***Glucocorticoid***
 receptors have been identified in human outflow tissue of the eye

AIMS. The purpose of this study, therefore, was to evaluate the serum concentration of total cortisol (TF), total testosterone (TT), free testosterone (FT), FSH (follicle stimulating hormone), LH (lutropin), ACTH (adrenocorticotropin), SHBG (sex hormone-binding globulin), DHEA-SO4 (dehydroepiandrosterone sulfate) as well as free cortisol (UFF) and 17-OHCS in 24 hours urinary samples in patients treated because of POAG. PATIENTS AND METHODS: Studies were performed in the group of 30 male patients, aged 55 +/- 13 years, treated because of ***glaucoma*** for more than two years. Serum and urinary concentration of hormones were studied using RIA methods (DPC). RESULTS: The serum concentration of TF (652.03 +/- 315.43 nmol/l), UFF (248.75 +/- 99.39 nmol/l) and 17-OHCS (5.47 +/- 2.64 mg/24 h) in urine was increased compared with control group. There was not significant difference in concentration of pituitary-gonadal axis hormones in glaucomatous and control groups of patients. CONCLUSION: The results could point to the fact that changes in the endocrine system are one of the factors involved in the pathogenesis of POAG. We conclude that an elevated level of cortisol, free cortisol and its metabolites is closely related to the POAG.

L8 ANSWER 3 OF 9 BIOSIS COPYRIGHT 2000 BIOSIS
 ACCESSION NUMBER: 1999:274116 BIOSIS
 DOCUMENT NUMBER: PREV199900274116
 TITLE: Glucocorticoid target receptors and isozymes of 11B-hydroxysteroid dehydrogenase in normal and glaucomatous human eyes.
 AUTHOR(S): Stokes, J. D.; Andrew, R. (1); Seckl, J. R. (1); O'Brien, C.
 CORPORATE SOURCE: (1) Dept. of Medicine, Western General Hospital, University of Edinburgh, Edinburgh UK
 SOURCE: IOVS, (March 15, 1999) Vol. 40, No. 4, pp. S669.
 Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology
 Fort Lauderdale, Florida, USA May 9-14, 1999 Association for Research in Vision and Ophthalmology

DOCUMENT TYPE: Conference
 LANGUAGE: English

L8 ANSWER 4 OF 9 MEDLINE
 ACCESSION NUMBER: 1999364864 MEDLINE
 DOCUMENT NUMBER: 99364864
 TITLE: Effects of glucocorticoids on the trabecular meshwork: towards a better understanding of ***glaucoma***
 AUTHOR: Wordinger R J; Clark A F
 CORPORATE SOURCE: Department of Anatomy and Cell Biology, University of North Texas, Health Science Center, Fort Worth 76107, USA
 SOURCE: PROGRESS IN RETINAL AND EYE RESEARCH, (1999 Sep) 18 (5) 629-67. Ref. 224
 Journal code: C2P ISSN: 1350-9462
 PUB. COUNTRY: ENGLAND: United Kingdom
 Journal, Article, (JOURNAL ARTICLE)
 General Review, (REVIEW)
 (REVIEW, ACADEMIC)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals

ENTRY MONTH: 199911
 ENTRY WEEK: 19991102
 AB Glucocorticoid effects on the human trabecular meshwork can be used as a model system in which to study glaucomatous damage to the trabecular meshwork. One of the most important risk factors for ***glaucoma*** is an elevated intraocular pressure. The administration of glucocorticoids also can cause elevated intraocular pressure in some individuals. In addition, there is suggestive evidence linking glucocorticoids with the development of ***glaucoma***. Glucocorticoids cause multiple effects on the human trabecular meshwork including changes in extracellular matrix metabolism, organisation of the cytoskeleton, and changes in gene expression and cell function. New discoveries on the molecular mechanisms of ***glucocorticoid*** ***receptor*** action provide new opportunities to study the possible role of this receptor in the development of ***glaucoma***. For example, alternate spliced forms of the ***glucocorticoid*** ***receptor***, ***glucocorticoid*** ***receptor*** response element half-sites, numerous modulatory factors, and direct effects of nuclear transcription factors have been recently described. Other recent information has shown that the new ***glaucoma*** gene (GLC1A/myocilin) is induced in the human trabecular meshwork by glucocorticoids. Although the exact function of myocilin is currently unknown, it offers the opportunity to dissect the molecular pathways regulating aqueous humor outflow. Future challenges include determining (1) which glucocorticoid effects in the human trabecular meshwork are responsible for elevated intraocular pressure, and (2) the significance of these findings to the development of ***glaucoma***.

L8 ANSWER 5 OF 9 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 1
 ACCESSION NUMBER: 1997:303241 BIOSIS
 DOCUMENT NUMBER: PREV199799602444
 TITLE: PCR-SSCP analysis of the glucocorticoid-responsive element of the atrial natriuretic peptide gene familial primary open-angle ***glaucoma***
 AUTHOR(S): Richardson, Kimberley A., Tunny, Terry J. (1), Clark, Charles V.
 CORPORATE SOURCE: (1) Univ. Dep. Med., Greenslopes Hosp., Brisbane, QLD 4120 Australia
 SOURCE: Clinical and Experimental Pharmacology and Physiology, (1997) Vol. 24, No. 6, pp. 427-429. ISSN: 0305-1870
 DOCUMENT TYPE: Article
 LANGUAGE: English
 AB 1. Familial primary open-angle ***glaucoma*** (POAG) is a heterogeneous disease of unknown aetiology and the elucidation of the underlying genetic mechanisms contributing to phenotypic expression will be essential if earlier diagnosis of at-risk individuals and more specific medical treatment can be achieved. In a significant percentage of patients with POAG, intraocular pressure increases in response to topical ocular glucocorticoids. 2. Atrial natriuretic peptide (ANP) assists in the regulation of intraocular pressure levels and binding of the

glucocorticoid ***receptor*** dimer to the glucocorticoid-responsive element in intron 2 of the ANP gene has been shown to increase ANP mRNA levels in vitro. We amplified and examined this sequence in the ANP gene by PCR-SSCP analysis in 100 patients with familial POAG and in 60 normal control subjects. No base alterations in the amplified product were found. Thus, the present study found no evidence for an alteration in the sequence of the glucocorticoid-responsive element of the ANP gene that could alter ANP gene transcription in patients with familial POAG. The mechanism responsible for the increase in intraocular pressure levels in response to glucocorticoids is most likely independent of the glucocorticoid-responsive element in the ANP gene.

L8 ANSWER 6 OF 9 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 96286937 SCISEARCH
THE GENUINE ARTICLE: U7853
TITLE: INHIBITION OF
DEXAMETHASONE-INDUCED CYTOSKELETAL
CHANGES

IN CULTURED HUMAN
TRABECULAR MESHWORK CELLS BY
TETRAHYDROCORTISOL

AUTHOR: CLARK A F, Wilson K; McCartney M
D, Miggins S T, Kunkle M;
WILSON K; Miggins S T;

MCCARTNEY M D
CORPORATE SOURCE: ALCON LABS INC,
GLAUCOMA RES R241, 6201 S FREEWAY, FT
WORTH, TX, 76134 (Reprint)

COUNTRY OF AUTHOR: USA
SOURCE: INVESTIGATIVE
OPHTHALMOLOGY & VISUAL SCIENCE, (APR
1996)

Vol. 37, No. 5, pp. 805-813.
ISSN: 0146-0404.

DOCUMENT TYPE: Article, Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 47

*ABSTRACT IS AVAILABLE IN THE
ALL AND IALL FORMATS*

AB Purpose, To determine the cellular mechanism
of action of the
intraocular pressure (IOP) lowering steroid
tetrahydrocortisol (THF).

Methods, Tetrahydrocortisol was evaluated for
glucocorticoid antagonist
activity using in vitro and in vivo assays.

Systemically administered THF
was evaluated for its ability to inhibit
dexamethasone-induced body weight
loss and systemic hypertension in rats. In vitro
receptor antagonism was
tested using the supernatant fraction of IM9 cells as
the source of

soluble ***glucocorticoid*** ***receptor***
in H-3-dexamethasone

displacement binding assays. In addition, six
different primary human
trabecular meshwork (TM) cell lines were cultured
for 0 to 14 days in the
absence or presence of dexamethasone (10(-7) M)
and/or THF (10(-6) to
10(-6) M). The effects of these steroids on the TM
cytoskeleton were
determined by epifluorescent microscopy and by
transmission electron
microscopy.

Results, Tetrahydrocortisol was unable to inhibit
the dexamethasone
(DEX)-induced systemic hypertension and decrease
in body mass in rats and
was unable to displace H-3-DEX from the soluble
human

glucocorticoid ***receptor***

However, THF inhibited the
DEX-induced formation of cross-linked actin

networks in cultured human TM
cells in a progressive and dose-dependent manner
(IC50 = 5.7 x 10(-7) M).
Dexamethasone caused changes in the TM cell
microtubules that were
reversed partially by concomitant treatment with
THF. Tetrahydrocortisol
alone appeared to increase microfilament bundling in
TM cells.

Conclusions, Tetrahydrocortisol was not a
glucocorticoid antagonist at
the level of the classical ***glucocorticoid***
receptor and
did not appear to antagonize systemically mediated
glucocorticoid activity
in the rat. Tetrahydrocortisol inhibited DEX-induced
changes in the TM
microfilaments and microtubules. These results may
explain partially the
IOP lowering activity of THF because
glucocorticoid-mediated changes in
the TM cytoskeleton have been proposed to be
involved in the generation of

ocular ***hypertension***

L8 ANSWER 7 OF 9 MEDLINE
DUPLICATE 2
ACCESSION NUMBER: 94131755 MEDLINE
DOCUMENT NUMBER: 94131755
TITLE: Glucocorticoid-induced formation of
cross-linked actin

networks in cultured human trabecular
meshwork cells

AUTHOR: Clark A F, Wilson K; McCartney M
D, Miggins S T, Kunkle M;
Howe W

CORPORATE SOURCE: Alcon Laboratories, Inc.,
Fort Worth, Texas 76134.

SOURCE: INVESTIGATIVE
OPHTHALMOLOGY AND VISUAL SCIENCE,
(1994 Jan)

35 (1) 281-94

Journal code: GWL ISSN: 0146-0404

PUB. COUNTRY: United States

Journal, Article, (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199405

AB PURPOSE: To determine the effects of

glucocorticoid treatment on the
microfilament structure of cultured human trabecular
meshwork cells

Topical or systemic administration of glucocorticoids
can lead to the

development of ***ocular***

hypertension and to the

development of vision loss, which is clinically

similar to primary open

angle ***glaucoma*** However, the

mechanism(s) by which

glucocorticoids cause ***ocular***

hypertension is not well

defined. Alterations in the trabecular meshwork, the

site of drainage of

aqueous humor from the eye, have been linked to the

development of

ocular ***hypertension***

METHODS. Human trabecular meshwork

cells were cultured in the presence and absence of

glucocorticoids for 0

to 21 days. The microfilament organization of the

cultured trabecular

meshwork cells was examined by epifluorescent and

transmission electron

microscopy. RESULTS. Glucocorticoids caused a

progressive change in the

organization of microfilaments in the trabecular

meshwork cells, but not

in other cultured ocular cells. By fluorescence

microscopic analysis, the

actin stress fibers found in control trabecular

meshwork cells were

reorganized on treatment with glucocorticoids into

cross-linked actin

networks that resembled geodesic-dome-like

polygonal lattices. The

cross-linked actin networks were reversible on

withdrawal of the

glucocorticoid treatment. Dose-response data for
dexamethasone, relative
ranking of activity with glucocorticoid potency, and
partial inhibition

with glucocorticoid antagonists all suggest the
involvement of the

trabecular meshwork ***glucocorticoid***

receptor in

cross-linked actin network formation. The

reorganization of the trabecular

meshwork cytoskeleton alters cell function because

glucocorticoid

treatment of cultured trabecular meshwork cells also

inhibited trabecular

meshwork cell migration and proliferation

CONCLUSION. The steroid-induced

alteration in trabecular meshwork cytoskeleton may

be an important factor

in the development of steroid-induced

ocular

hypertension and may play a role in the

ocular

hypertension associated with primary open

angle ***glaucoma***

L8 ANSWER 8 OF 9 MEDLINE

DUPLICATE 3

ACCESSION NUMBER: 91201034 MEDLINE

DOCUMENT NUMBER: 91201034

TITLE: Increased plasma noncortisol

glucocorticoid activity in

open-angle ***glaucoma*** [published

erratum appears in

Invest Ophthalmol Vis Sci 1991

Jul;32(8);2440]

AUTHOR: McCarty G R, Schwartz B

CORPORATE SOURCE: Department of

Ophthalmology, New England Medical Centre

Hospitals, Boston, Massachusetts 02111

CONTRACT NUMBER: EY00024 (NEI)

EY07045 (NEI)

SOURCE: INVESTIGATIVE

OPHTHALMOLOGY AND VISUAL SCIENCE,

(1991 Apr)

32 (5) 1600-8.

Journal code: GWL ISSN: 0146-0404

PUB. COUNTRY: United States

Journal, Article, (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199107

AB Total biologic plasma glucocorticoid activity of

normal, ocular

hypertensive, and open-angle ***glaucoma***

patients was compared

using a ***glucocorticoid*** ***receptor***

-based competitive

binding assay. Multiple linear-regression analysis

was used to adjust for

the effects of significant ocular and nonocular

variables, including

therapy for ***glaucoma***. The

glaucoma patients had

significantly greater plasma glucocorticoid activities

than did normal

subjects. A comparison of receptor-based assay

values to values obtained

with a cortisol radioimmunoassay showed that

significant amounts of

biologic glucocorticoid activity in the plasma of the

glaucoma

patients could not be explained by cortisol alone. In

the normal and

ocular hypertensive groups, however, virtually all of

the plasma

glucocorticoid activity could be accounted for by

cortisol. These results

suggest that in open-angle ***glaucoma***

patients, noncortisol

glucocorticoids are responsible for elevating biologic

plasma

glucocorticoid activity. Thus, open-angle

glaucoma may be

associated with a disturbance of the

hypothalamic-pituitary-adrenal axis

that produces increased plasma levels of both

cortisol and other

noncortisol glucocorticoids

L8 ANSWER 9 OF 9 MEDLINE

DUPLICATE 4

ACCESSION NUMBER: 84017537 MEDLINE

DOCUMENT NUMBER: 84017537

TITLE: Potentiation of glucocorticoid activity by 5

beta-dihydrocortisol: its role in

glaucoma

AUTHOR: Weinstein B I; Gordon G G;

Southren A L

CONTRACT NUMBER: EY 01313 (NEI)

SOURCE: SCIENCE, (1983 Oct 14) 222

(4620) 172-3.

Journal code UJ7 ISSN: 0036-8075

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals, Cancer

Journals

ENTRY MONTH: 198401

AB 5 beta-Dihydrocortisol potentiated the threshold level (the smallest dose

producing a measurable effect) of topically applied cortisol (0.02

percent) and dexamethasone (0.003 percent) in

causing nuclear

translocation of the cytosolic ***glucocorticoid***

receptor

in rabbit iris-ciliary body tissue 5

beta-Dihydrocortisol accumulates in

cells cultured from trabecular meshwork specimens

from patients with

primary open-angle ***glaucoma***, but not in

similar cells derived

from nonglaucomatous patients. In view of the

sensitivity of patients with

primary open-angle ***glaucoma*** to the

effects of glucocorticoids in

raising intraocular pressure, this potentiation may be

responsible for the

steroid sensitivity and for the ***ocular***

hypertension

seen in this disorder.

=> d ibib abs 16 1-40

L6 ANSWER 1 OF 40 WPIDS COPYRIGHT 2000

DERWENT INFORMATION LTD

ACCESSION NUMBER: 2000-491060 [43]

WPIDS

DOC NO. CPI: C2000-147602

TITLE: Diagnosis, prognosis and treatment of

glaucoma

based on detecting specific

polymorphisms in the promoter

of the trabecular meshwork inducible

glucocorticoid ***receptor***

gene.

DERWENT CLASS: B04 D16

INVENTOR(S): CHEN, H, CHEN, P,

NGUYEN, T D, POLANSKY, J R

PATENT ASSIGNEE(S): (REGC) UNIV

CALIFORNIA

COUNTRY COUNT: 89

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2000042220 A1 20000720 (200043)* EN 121

RW: AT BE CH CY DE DK EA ES FI FR GB

GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SL SZ TZ UG ZW

W AE AL AM AT AU AZ BA BB BG BR BY

CA CH CN CR CU CZ DE DK DM EE ES

FI GB GD GE GH GM GR HU ID IL IN IS JP

KE KG KP KR KZ LC LK LR LS

LT LU LV MA MD MG MK MN MW MX

NO NZ PL PT RO RU SD SE SG SI SK SL

TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

APPLICATION DETAILS

PATENT NO KIND APPLICATION

DATE

WO 2000042220 A1

WO 2000-US559

20000111

PRIORITY APPLN. INFO US 1999-306828

19990507; US 1999-227881

19990111

AN 2000-491060 [43] WPIDS

AB WO 200042220 A UPAB: 20000907

NOVELTY - A method for the diagnosis, prognosis

and treatment of

glaucoma, based on detecting specific

polymorphisms in the

promoter of the trabecular meshwork inducible

glucocorticoid

receptor gene, is new

DETAILED DESCRIPTION - Diagnosis, or

prognosis, of ***glaucoma***

comprises incubating a marker nucleic acid (I) that

hybridizes

specifically with a polynucleotide linked to a TIGR

(trabecular meshwork

inducible ***glucocorticoid*** ***receptor***

) promoter with

complementary nucleic acid (II) present in a patient's

cell or body fluid

sample. (I) and (II) hybridize and a polymorphism is

detected that is:

(i) predictive of a mutation affecting TIGR

response, and

(ii) diagnostic (prognostic) of ***glaucoma***

INDEPENDENT CLAIMS are also included for the following.

(a) a similar method for diagnosing sensitivity to

steroids,

(b) a nucleic acid (III) that comprises any of the

sequences (N1)

(5300 bp (base pairs)), (N3) (6169 bp), (N4) (926

bp), (N5) (2099 bp) or

(N24) (1548 bp);

(c) a recombinant DNA (IIIa) that hybridizes

specifically to the

sequences of (b);

(d) a pure molecule (IV) that binds to (III);

(e) a pure molecule (IVa) that binds to any of

about 40 specified

nucleic acids that include a cis-element;

(f) a method for the treatment of

glaucoma by administering

an agent that binds a cis-element present in (N1);

(g) a nucleic acid (IIIb) that is a region of (N33)

which comprises

the sequence CAAACAGACTTCCGGAAGGT;

(h) a nucleic acid (IIIc) that hybridizes

specifically to (IIIb);

(i) a vector or cell containing (IIIb);

(j) a method for detecting the characteristic

TIGRmt11 sequence by

hybridization to labeled (IIIb), for detecting

increased susceptibility to

glaucoma, progressive ocular hypertensive

disease or steroid

sensitivity;

(k) a kit for method OF (j) containing labeled

(IIIb) and system for

detecting hybridization;

(l) a nucleic acid (IIId) that is (N1), (N3), (N2)

(5304 bp) or (N34)

(5271 bp) or any of their fragments that contain a

functional regulatory

sequence;

(m) cells or vectors containing (IIIId);

(n) a method for detecting the TIGRmt11

sequence variant by

amplification;

(o) kit for method of (n) containing amplification

primers and

enzyme;

(p) a method for detecting a polymorphism in the

5'-flanking region

of TIGR by amplification with specific primers

(sequences reproduced in

specification);

(q) the nucleic acids (N37) (283 bp) and (N38)

(227 bp), sequences

95% identical with them or their variants,

(r) recombinant nucleic acids, vectors and cells

containing the

sequences of (q);

(s) identification of a protein or compound that

binds to, and

modifies expression of, TIGR from ability to bind to

(N37), (N38) or their

variants, or to regions of (N3) or (N34);

(t) a method for identifying a compound that

modulates the binding

reaction in (s); and

(u) a method for identifying compounds that

modulate steroid

induction of a TIGR gene.

ACTIVITY - Antiglaucoma; ophthalmic

No data given.

MECHANISM OF ACTION - Modulation of

expression of the TIGR gene

USE - The method is used for diagnosis and

prognosis of glaucoma (of

all types), steroid sensitivity and progressive ocular

hypertension that

leads to loss of vision. Also glaucoma can be treated

by administering an

agent that binds to cis-acting elements within the

TIGR promoter. The TIGR

promoter (or other regulatory regions) can be used to

express homologous

or heterologous genes, particularly for tissue-specific

expression of

therapeutic transgenes for treating glaucoma, also to

generate transgenic

animals and in screening for compounds (specific

modulators) with

diagnostic or therapeutic potential. Fragments of the

TIGR sequence can be

used as amplification primers or probes, e.g. for

isolating related

sequences in non-human animals.

Dwg 0/9

L6 ANSWER 2 OF 40 WPIDS COPYRIGHT 2000

DERWENT INFORMATION LTD

ACCESSION NUMBER: 2000-205642 [18]

WPIDS

DOC NO. CPI: C2000-063422

TITLE: Novel glucocorticoid and thyroid

hormone receptor ligands

useful for treating diabetes, inflammation

and obesity.

DERWENT CLASS: B05

INVENTOR(S): APELQVIST, T, GOEDE, P,

HOLMGREN, E

PATENT ASSIGNEE(S): (KARO-N) KAROBIO

AB, (KARO-N) KARO BIO AB

COUNTRY COUNT: 86

PATENT INFORMATION

PATENT NO KIND DATE WEEK LA PG

WO 2000007972 A1 20000217 (200018)* EN 54

RW: AT BE CH CY DE DK EA ES FI FR GB

GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SL SZ UG ZW

W AE AL AM AT AU AZ BA BB BG BR BY

CA CH CN CU CZ DE DK EE ES FI GB

GD GE GH GM HR HU ID IL IN IS JP KE KG

KP KR KZ LC LK LR LS LT LU

LV MD MG MK MN MW MX NO NZ PL PT

RO RU SD SE SG SI SK SL TJ TM TR

TT UA UG US UZ VN YU ZA ZW

AU 9951881 A 20000228 (200030)

APPLICATION DETAILS

PATENT NO KIND APPLICATION

DATE

WO 2000007972 A1

WO 1999-IB1447

19990804

AU 9951881 A

AU 1999-51881

19990804

FILING DETAILS:

PATENT NO KIND PATENT NO

AU 9951881 A Based on WO 200007972

PRIORITY APPLN INFO GB 1998-16935
19980805

AN 2000-205642 [18] WPIDS
AB WO 20007972 A UPAB 20000412

NOVELTY - Novel liver-selective
glucocorticoid ***receptor***
antagonists are useful for the treatment of metabolic disorders

DETAILED DESCRIPTION - Diphenyl
compounds of formula (I) and their
salts and stereoisomers are new
R1 = aliphatic hydrocarbyl, aromatic hydrocarbyl,
carboxylic acid or
its ester, alkenyl carboxylic acid or its ester, OH,
halo or CN;
R2, R3 = H, halo, 1-4C alkyl or 3-5C cycloalkyl,
provided that at
least one is not H,
X = CO or CH2;

R4 = aliphatic, aromatic, or heteroaromatic,
R5 = halo, 1-4C alkyl or 3-5C cycloalkyl;
Y = OH, OMe, amuno or alkylamino, and
n = 0-4.

ACTIVITY - Antidiabetic, Antiinflammatory,
Endocrine-Gen;
Antiarteriosclerotic; Antiarrhythmic, Antidepressant,
Osteopathic;

Antilipemic; Anorectic, Ophthalmological
MECHANISM OF ACTION -

Glucocorticoid - ***Receptor***
-Antagonist, Thyroid-Receptor-Antagonist.

USE - (I) are useful for preventing, inhibiting or
treating diseases
associated with a metabolism dysfunction or which is
dependent on the
expression of a ***glucocorticoid***
receptor regulated gene
such as diabetes, Cushing's syndrome, inflammation,
hypercholesterolemia,
obesity, skin disorders, ***glaucoma*** or other
endocrine disorders
related to thyroid hormone (claimed). (I) are also
useful for treating
atherosclerosis, cardiac arrhythmias, depression,
osteoporosis,
hypothyroidism, thyroid cancer as well as
glaucoma and
congestive heart failure.

ADVANTAGE - (I) are preferably liver
selective
Dwg. 0/0

L6 ANSWER 3 OF 40 EMBASE COPYRIGHT
2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000276535 EMBASE
TITLE: Assessment of therapeutic index of
inhaled steroids.

AUTHOR: Israel E.
CORPORATE SOURCE: E. Is. ael, Div. Pulmonary
Critical Care Med., Brigham
Womens Hospital, Harvard Medical
School, Boston, MA 02115,
United States

SOURCE: Lancet, (12 Aug 2000) 356/9229
(527-528)

Refs: 4
ISSN: 0140-6736 CODEN: LANCAO

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal, Note
FILE SEGMENT 006 Internal Medicine
015 Chest Diseases, Thoracic Surgery
and Tuberculosis
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English

L6 ANSWER 4 OF 40 BIOSIS COPYRIGHT 2000
BIOSIS
ACCESSION NUMBER: 2000 402241 BIOSIS
DOCUMENT NUMBER: PREV200000402241
TITLE: The genetics of open-angle
glaucoma The story of
GLC1A and myocilin
AUTHOR(S): Alward, Wallace L. M. (1)
CORPORATE SOURCE: (1) Department of

Ophthalmology, University of Iowa College
of Medicine, 200 Hawkins Drive, Iowa
City, IA, 52242-1091
USA

SOURCE: Eye (London), (June, 2000) Vol. 14,
No. 3B, pp. 429-436
print
ISSN: 0950-222X

DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A linkage analysis study was performed on a single
large family with
juvenile-onset primary open-angle
glaucoma (POAG). This led to
the recognition that there was a region of
chromosome 1q that harboured a
gene for juvenile-onset POAG. This chromosomal
site was called GLC1A. It
was discovered that a gene that produces the protein
myocilin resides
within this interval and that mutations in myocilin
caused most cases of
autosomal dominant juvenile-onset POAG. More
importantly myocilin
mutations also cause up to 4.6% of cases of
adult-onset POAG. The
prevalence of myocilin mutations is similar
regardless of race or
geographic location. There are widely variable
glaucoma
phenotypes depending on the specific mutation in
myocilin. Myocilin is
expressed in multiple tissues throughout the eye and
in many other organs.
In the trabecular meshwork the production of
myocilin can be induced by
the application of topical corticosteroids. The exact
function of myocilin
in health and disease remains a mystery.

L6 ANSWER 5 OF 40 MEDLINE
ACCESSION NUMBER: 2000414284 MEDLINE
DOCUMENT NUMBER: 20388270

TITLE: [Hormonal changes in male patients
with primary open angle

glaucoma].
Ocena zmian hormonalnych u mezczyzn
chorych na jaskrze

prosta otwartego kata przesaczania.
AUTHOR: Nowak M, Swietochowska E,
Jochan K, Buntner B
CORPORATE SOURCE: Zakladu Patofizjologii i
Endokrynologii Slaskiej AM w
Zabrze.

SOURCE: KLINIKA OCZNA, (2000) 102 (2)
103-8

Journal code: KWC. ISSN: 0023-2157.
PUB. COUNTRY: Poland
Journal, Article, (JOURNAL ARTICLE)

LANGUAGE: Polish
ENTRY MONTH: 200011
ENTRY WEEK: 20001101
AB INTRODUCTION: Primary open angle
glaucoma (POAG) is the most
common type of ***glaucoma***, pathogenesis
of which is not completely
known. Several clinical studies show that
glucocorticoid hormones may be
implicated in the pathogenesis of POAG and ocular
hypertension.

Glucocorticoid ***receptors*** have
been identified in human
outflow tissue of the eye. AIMS: The purpose of this
study, therefore, was
to evaluate the serum concentration of total cortisol
(TF), total
testosterone (TT), free testosterone (FT), FSH
(foliotropin), LH
(lutropin), ACTH (adrenocorticotropin), SHBG (sex
hormone-binding
globulin), DHEA-SO4 (dehydroepiandrosterone
sulfate) as well as free
cortisol (UFF) and 17-OHCS in 24 hours urinary
samples in patients treated
because of POAG. PATIENTS AND METHODS
Studies were performed in the group
of 30 male patients, aged 55 +/- 13 years, treated

because of

glaucoma for more than two years. Serum
and urinary concentration
of hormones were studied using RIA methods
(DPC). RESULTS: The serum
concentration of TF (652.03 +/- 315.43 nmol/l), UFF
(248.75 +/- 99.39
nmol/l) and 17-OHCS (5.47 +/- 2.64 mg/24 h) in
urine was increased
compared with control group. There was not
significant difference in
concentration of pituitary-gonadal axis hormones in
glaucomatous and
control groups of patients. CONCLUSION: The
results could point to the
fact that changes in the endocrine system are one of
the factors involved
in the pathogenesis of POAG. We conclude that an
elevated level of
cortisol, free cortisol and its metabolites is closely
related to the
POAG.

L6 ANSWER 6 OF 40 EMBASE COPYRIGHT
2000 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1999390306 EMBASE
TITLE: A cellular assay distinguishes normal
and mutant

TIGR/myocilin protein.

AUTHOR: Zhou Z., Vollrath D.
CORPORATE SOURCE: D Vollrath, Department of
Genetics, Stanford University
School Medicine, Lane Building, 300

Pasteur Drive,
Stanford, CA 94305-5120, United States
vollrath@genome.stanford.edu

SOURCE: Human Molecular Genetics, (1999)
8/12 (2221-2228).

Refs: 49
ISSN: 0964-6906 CODEN: HMGEES

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal, Article
FILE SEGMENT: 012 Ophthalmology
022 Human Genetics
029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English
AB ***Glaucoma*** is a blinding eye disease that
affects approx

70,000,000 people world-wide. Mutations in the
gene TIGR/MYOC have been
shown to cause the most common form of the
disease, primary open angle

glaucoma, in selected families. Amino
acid sequence variants of
the gene have been found in 2-4% of sporadic
primary open angle

glaucoma cases. Most variants are rare and
it is often difficult

to definitively distinguish between a deleterious
mutation and a benign
variant solely on the basis of relative frequencies in
patient and control

groups. The function of the TIGR/myocilin protein
is unknown and an assay

to functionally classify variants is lacking. We sought
to develop a

biochemical assay to distinguish different forms of
TIGR/myocilin. We

investigated the Triton X-100 detergent solubility
characteristics of

mutant and normal forms of the protein, expressed
by transfection in

cultured cells. We observed a clear difference in the
behavior of the two

types of TIGR/myocilin, all confirmed mutant
proteins tested were

substantially Triton insoluble, while normal protein
and controls were

completely soluble. We also tested seven ambiguous
variant proteins and

classified them as mutant or normal on the basis of
their Triton

solubility. The results in some cases validated, and
in other cases

contradicted, earlier classifications of these variants.
To our knowledge,

Triton solubility is the first example of a general

difference in the properties of mutant and normal forms of TIGR/myocilin. The assay we have developed will be useful for discerning protein functional information from the location of mutations, will aid genetic counseling of individuals with TIGR/myocilin variants and may provide a clue to understanding a mechanism by which mutations in TIGR/MYOC cause ***glaucoma***

L6 ANSWER 7 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1999 274116 BIOSIS
DOCUMENT NUMBER: PREV199900274116
TITLE: Glucocorticoid target receptors and isozymes of

11B-hydroxysteroid dehydrogenase in normal and glaucomatous human eyes

AUTHOR(S): Stokes, J. D.; Andrew, R. (1); Seckl, J. R. (1); O'Brien, C.

CORPORATE SOURCE: (1) Dept. of Medicine, Western General Hospital, University of Edinburgh, Edinburgh UK

SOURCE: IOVS, (March 15, 1999) Vol. 40, No. 4, pp. S669.

Meeting Info. Annual Meeting of the Association for Research in Vision and Ophthalmology Fort Lauderdale, Florida, USA May 9-14, 1999 Association for Research in Vision and Ophthalmology

DOCUMENT TYPE: Conference
LANGUAGE: English

L6 ANSWER 8 OF 40 MEDLINE
DUPLICATE 1
ACCESSION NUMBER: 1999364864 MEDLINE
DOCUMENT NUMBER: 99364864
TITLE: Effects of glucocorticoids on the trabecular meshwork

towards a better understanding of ***glaucoma***

AUTHOR: Wordinger R J, Clark A F
CORPORATE SOURCE: Department of Anatomy and Cell Biology, University of North Texas, Health Science Center, Fort Worth 76107, USA.

rworthing@hsc.unt.edu
SOURCE: PROGRESS IN RETINAL AND EYE RESEARCH, (1999 Sep) 18 (5) 629-67. Ref. 224

Journal code: C2P. ISSN: 1350-9462
PUB. COUNTRY: ENGLAND: United Kingdom
Journal, Article, (JOURNAL ARTICLE)
General Review, (REVIEW)
(REVIEW, ACADEMIC)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY WEEK: 19991102

AB Glucocorticoid effects on the human trabecular meshwork can be used as a model system in which to study glaucomatous damage to the trabecular meshwork. One of the most important risk factors for ***glaucoma*** is an elevated intraocular pressure. The administration of glucocorticoids also can cause elevated intraocular pressure in some individuals. In addition, there is suggestive evidence linking glucocorticoids with the development of ***glaucoma***. Glucocorticoids cause multiple effects on the human trabecular meshwork including changes in extracellular matrix metabolism, organization of the cytoskeleton, and changes in gene expression and cell function. New discoveries on the molecular mechanisms of ***glucocorticoid*** ***receptor*** action provide new

opportunities to study the possible role of this receptor in the development of ***glaucoma***. For example, alternate spliced forms of the ***glucocorticoid*** ***receptor***, ***glucocorticoid*** ***receptor*** response element half-sites, numerous modulatory factors, and direct effects of nuclear transcription factors have been recently described. Other recent information has shown that the new

glaucoma gene (GLC1A/myocilin) is induced in the human trabecular meshwork by glucocorticoids. Although the exact function of myocilin is currently unknown, it offers the opportunity to dissect the molecular pathways regulating aqueous humor outflow. Future challenges include determining (1) which glucocorticoid effects in the human trabecular meshwork are responsible for elevated intraocular pressure; and (2) the significance of these findings to the development of ***glaucoma***.

L6 ANSWER 9 OF 40 MEDLINE
DUPLICATE 2
ACCESSION NUMBER: 2000016770 MEDLINE
DOCUMENT NUMBER: 20016770

TITLE: [Mechanism of action of glucocorticoids in asthma].

Les mecanismes d'action moleculaire des glucocorticoides dans l'asthme

AUTHOR: Jaffuel D, Mathieu M, Godard P, Michel F B, Demoly P
CORPORATE SOURCE: Service des Maladies Respiratoires, INSERM U454, Hopital Arnaud-de-Villeneuve, CHU de Montpellier.

SOURCE: REVUE DES MALADIES RESPIRATOIRES, (1999 Sep) 16 (4) 431-42.

Ref. 122
Journal code: RZ9. ISSN: 0761-8425.

PUB. COUNTRY: France
Journal, Article, (JOURNAL ARTICLE)
General Review, (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY WEEK: 20000204

AB While on the basis of clinical studies glucocorticoids (GC) became the first-line therapy for asthma, the molecular basis of GC action has been extensively studied. Glucocorticoids exert their effects by binding to the ***glucocorticoid*** ***receptor*** (GR), which then inhibits or increases gene transcription through processes known as transrepression and transactivation, respectively. Transrepression results from the inhibitory interaction between the GR and other transcription factors like AP-1 and NF-kappa B. Since AP-1 and NF-kappa B DNA binding sites have been mapped to the promoter regions of many genes coding for proinflammatory mediators (IL-1, 2, 5, 6, 8, 13, TNF-alpha, RANTES, Eotaxin, GM-CSF, metalloproteinases, ICAM-1 ...), this interaction may be an important aspect of the GC anti-inflammatory properties. Transactivation is mediated through binding of the GC-activated GR to a DNA sequence called glucocorticoid response element (GRE) and may result in some benefits and side effects since GRE has been mapped to the promoter regions of genes coding for lipocortin, beta 2-adrenergic receptor, and for genes involved in the onset of metabolic effects (diabetes, hypokalemia, hyponatremia).

retention) and ***glaucoma***. Other molecular mechanisms may also be involved like the binding to the GR to a negative GRE (nGRE), the interaction with the basal transcriptional machinery, and the post transcriptional modulation of mRNA stability. In asthma, the relative importance of each mechanism remains to be studied, but both mechanisms may probably be involved.

L6 ANSWER 10 OF 40 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999 537359 CAPLUS
DOCUMENT NUMBER: 132 34173
TITLE: The preliminary study of ***glucocorticoid***

receptor gene in Chinese patients with glucocorticoid-induced

glaucoma
AUTHOR(S): Zhuo, Yehong, Ge, Jian, Guo, Yan, Lin, Mingkai

CORPORATE SOURCE: Zhongshan Ophthalmic Center, Sun Yat-sen University of Medical Sciences, Canton, 510060,

Peop. Rep. China
SOURCE: Eye Sci. (1999), 15(1), 46-50
CODEN: YAXUE3, ISSN: 1000-4432

PUBLISHER: Zhongshan Ophthalmic Center
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To study the ***glucocorticoid*** ***receptor*** (GR) and the associated gene regulation in the pathogenesis of glucocorticoid-induced

glaucoma (GIG) in Chinese patients. The trabecular cells of normal individuals and patients with GIG were cultured in vitro. By using polymerase chain reaction (PCR), gene fragments on GR DNA binding sites of trabecular cells were amplified. The product was detected by gel electrophoresis. The trabecular cells were cultured successfully in normal individuals and patients with GIG in vitro. A single PCR product was obtained in both two groups with the same size of 545 base pairs.

There is not any difference in gene on the GR DNA binding sites between normal individuals and patients with GIG. The results suggest the difference might be in mRNA or other functional genes.

REFERENCE COUNT: 9
REFERENCE(S): (1) Alvarad, J, Invest Ophthalmol Vis Sci 1992, V33, P1120
(2) Bloom, E, J Steroid Biochem 1980, V12, P175 CAPLUS
(3) Fancois, J, Ann Ocul 1954, V187, P805

(4) Holler, S, Science 1985, V318, P635
(5) Jian, G, Eye Science 1996, V12, P64
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 40 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD DUPLICATE 3

ACCESSION NUMBER: 1998-333347 [29]
WPIDS
DOC. NO. CPI: C1998-103395
TITLE: Diagnosing ***glaucoma*** and determining usefulness

of therapeutic agents - by detecting aberrant expression of beta ***glucocorticoid***

receptor
DERWENT CLASS: B04 D16
INVENTOR(S): CLARK, A F, WORDINGER, R J
PATENT ASSIGNEE(S): (CLAR-I) CLARK A F, (WORD-I) WORDINGER R J
COUNTRY COUNT: 23

PATENT INFORMATION

PATENT NO KIND DATE WEEK LA PG
 WO 9824932 A1 19980611 (199829)* EN 5
 RW AT BE CH DE DK ES FI FR GB GR IE IT
 LU MC NL PT SE
 W AU CA JP MX US
 AU 9852617 A 19980629 (199845)
 EP 943014 A1 19990922 (199943) EN
 R AT BE CH DE DK ES FI FR GB GR IE IT LI
 LU MC NL PT SE

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION DATE
WO 9824932 A1		WO 1997-US21054
19971114		
AU 9852617 A		AU 1998-52617
19971114		
EP 943014 A1		EP 1997-947569
19971114		
		WO 1997-US21054 19971114

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9852617 A	Based on	WO 9824932
EP 943014 A1	Based on	WO 9824932

PRIORITY APPLN INFO: US 1996-33227
 19961205
 AN 1998-333347 [29] WPIDS
 AB WO 9824932 A UPAB: 19980722
 Diagnosing ***glaucoma*** comprises either:
 (i) detecting aberrant ***glucocorticoid***
 receptor
 (GR) beta expression or defects in a GR gene which encodes GR beta ;
 (ii) detecting genetic changes in the GR gene leading to altered GR beta expression, or
 (iii) detecting genetic changes outside the GR gene which lead to altered GR beta expression.
 Also claimed is a method for determining whether an agent is useful for treating ***glaucoma*** by determining whether it interacts with GR beta or alters the expression of GR beta
 USE - Cultured human trabecular meshwork cell lines derived from glaucomatous donors express mRNA for both on alternate splice form of the human ***glucocorticoid*** ***receptor*** (GR beta), as well as the normal glucocorticoid receptor (GR alpha), whereas normal tm cell lines only express mRNA for GR alpha .
 Determining that an individual abnormally expresses GR beta in their trabecular meshwork or other tissues can lead to a diagnosis of ***glaucoma***
 Agents that have therapeutic value for treating ***glaucoma*** can be determined by using ligand binding assays or GR beta functional assays
 Dwg.0/0

L6 ANSWER 12 OF 40 WPIDS COPYRIGHT 2000
 DERWENT INFORMATION LTD
 ACCESSION NUMBER 1998-437038 [37]
 WPIDS
 DOC NO CPI: C1998-132799
 TITLE: New 16-hydroxy-11-substituted phenyl-4,9-oestradiene derivatives - having anti-glucocorticoid activity,
 prepared by dehydrating new 5 alpha-hydroxy-9-oestrone precursors.
 DERWENT CLASS B01
 INVENTOR(S) GEBHARD, R; GROEN, M B
 PATENT ASSIGNEE(S) (ALKU) AKZO NOBEL

NV
 COUNTRY COUNT 70
 PATENT INFORMATION

PATENT NO KIND DATE WEEK LA PG
 WO 9831702 A1 19980723 (199837)* EN 27
 RW AT BE CH DE DK EA ES FI FR GB GH
 GM GR IE IT KE LS LU MC MW NL OA
 PT SD SE SZ UG ZW
 W AM AU BB BG BR BY CA CN CZ EE GE
 HU ID IS JP KG KP KR LK LR LT LV
 MD MG MN MX NO NZ PL RO RU SG SI
 SK TR TT UA US UZ VN
 ZA 9800084 A 19980930 (199844) 26
 AU 9862935 A 19980807 (199901)
 NO 9903459 A 19990907 (199947)
 CZ 9902534 A3 20000112 (200009)
 EP 973792 A1 20000126 (200010) EN
 R: AT BE CH DE DK ES FI FR GB GR IE IT LI
 LU MC NL PT SE
 BR 9807079 A 20000418 (200032)
 CN 1248262 A 20000322 (200032)
 US 6072068 A 20000606 (200033)
 NZ 336790 A 20000623 (200038)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION DATE
WO 9831702 A1		WO 1998-EP377
19980113		
ZA 9800084 A		ZA 1998-84
19980106		
AU 9862935 A		AU 1998-62935
19980113		
NO 9903459 A		WO 1998-EP377
19980113		
CZ 9902534 A3		NO 1999-3459 19990714
19980113		WO 1998-EP377
EP 973792 A1		CZ 1999-2534 19980113
19980113		EP 1998-906887
BR 9807079 A		WO 1998-EP377 19980113
19980113		BR 1998-7079
CN 1248262 A		WO 1998-EP377 19980113
19980113		CN 1998-802618
US 6072068 A		WO 1998-EP377
19980113		
NZ 336790 A		US 1999-341603 19990714
19980113		NZ 1998-336790
		WO 1998-EP377 19980113

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9862935 A	Based on	WO 9831702
CZ 9902534 A3	Based on	WO 9831702
EP 973792 A1	Based on	WO 9831702
BR 9807079 A	Based on	WO 9831702
US 6072068 A	Based on	WO 9831702
NZ 336790 A	Based on	WO 9831702

PRIORITY APPLN INFO: EP 1997-200098
 19970115
 AN 1998-437038 [37] WPIDS
 AB WO 9831702 A UPAB: 19991122
 11-substituted-phenyl-oestra-4,9-diene compounds of formula (I), and their salts and solvates, and precursors of formula (II) are new R1 = 1-6C alkyl, 3-6C cycloalkyl, 1-6C alkoxy, triplate, pyridyl or phenyl (optionally substituted by one or more of CN, halogen and 1-4C alkyl), R2 = H, 1-6C alkyl, 1-oxo-(1-6C alkyl) or carboxy-1-oxo-(1-6C alkyl), R3 = H, halogen or 1-6C alkyl (optionally substituted by one or more of halogen and 1-6C alkoxy), R4 = H, 1-6C alkyl, 1-oxo-(1-6C alkyl) or carboxy-1-oxo-(1-6C alkyl), X = (H,OH), = O, or =

NOH, R5 = as R4 or a protected R4 group, P = protected keto
 USE - (I) have highly selective affinity for ***glucocorticoid***
 receptors and have potent in vivo anti-glucocorticoid activity
 They are used in the treatment or prophylaxis of glucocorticoid-dependent diseases (claimed), e.g. Cushing syndrome, diabetes, ***glaucoma***, sleep disturbances, depression, anxiety, atherosclerosis, hypertension, obesity, osteoporosis, addiction, withdrawal symptoms, Alzheimer's disease, schizophrenia, mania, hyperactivity, substance abuse and emesis.
 (II) are intermediates for (I)
 Dwg.0/0

L6 ANSWER 13 OF 40 BIOSIS COPYRIGHT 2000
 BIOSIS
 ACCESSION NUMBER 1998 243274 BIOSIS
 DOCUMENT NUMBER: PREV199800243274
 TITLE: A characterization of ***glucocorticoid***
 receptor on lymphocytes in patients with glucocorticoid-induced ***glaucoma*** (GIG).
 AUTHOR(S) Ge, J., Zhou, Y.; Lin, M.; Guo, Y.
 CORPORATE SOURCE: Zhongshan Ophthalmic Cent., Sun Yat-sen Univ Med Sci, Guangzhou 510060 China
 SOURCE: IOVS, (March 15, 1998) Vol. 39, No. 4, pp. S931.
 Meeting Info. Annual Meeting of the Association for Research in Vision and Ophthalmology Fort Lauderdale, Florida, USA May 10-15, 1998 Association for Research in Vision and Ophthalmology
 DOCUMENT TYPE: Conference
 LANGUAGE: English

L6 ANSWER 14 OF 40 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B V
 ACCESSION NUMBER: 1998095893 EMBASE
 TITLE: Novel mutations in the TIGR gene in early and late onset open angle ***glaucoma***
 AUTHOR: Mansergh F.C.; Kenna P.F.; Ayuso C.; Kiang A.-S.; Humphries P.; Farrar G.J.
 CORPORATE SOURCE: F.C. Mansergh, Wellcome Ocular Genetics Unit, Dept. of Genetics, Trinity College, Dublin 2, Ireland.
 fmnsergh@biotech bio ted ie
 SOURCE: Human Mutation, (1998) 11/3 (244-251)
 Refs: 16
 ISSN: 1059-7794 CODEN HUMUE3

COUNTRY: United States
 DOCUMENT TYPE: Journal, Article
 FILE SEGMENT: 012 Ophthalmology 022 Human Genetics
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 AB A gene for juvenile onset, open angle ***glaucoma*** (JOAG) has been localized to chromosome 1q21-31 in several families. Mutations in the trabecular meshwork-induced glucocorticoid response protein (TIGR) gene, which maps to this region, recently have been found in families segregating both JOAG and a later onset form of primary open angle ***glaucoma*** (POAG). We have analysed the TIGR gene in two families, one Spanish family segregating autosomal dominant JOAG and an Irish family with a later onset form of autosomal dominant POAG. We have found a G-T transversion in the first base of codon 426 in all affected members of the

Spanish family, which results in a valine to phenylalanine amino acid substitution. We have also found a G-A transition at the first base of codon 367 that segregates through all but one branch of the Irish family and results in a glycine to arginine amino acid substitution. Members of this family that carry the Gly367Arg change also share a common haplotype that is neither present in any of the unaffected members of the family, nor in the branch that does not segregate the mutation. Identification of further mutations in the TIGR gene increases its importance in the etiology of open angle ***glaucoma***

L6 ANSWER 15 OF 40 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999-52236 CAPLUS
DOCUMENT NUMBER: 130-247174
TITLE: Characterization of ***glucocorticoid***

receptor on lymphocytes in Chinese patients with glucocorticoid-induced ***glaucoma***
AUTHOR(S): Zhuo, Yehong, Ge, Jian, Guo, Yan
CORPORATE SOURCE: Zhongshan Ophthalmic Center, Sun Yat-sen University of Medical Sciences, Canton, 510060, Peop. Rep. China

SOURCE: Eye Sci. (1998), 14(3), 145-148
CODEN: YAXUE3; ISSN: 1000-4432
PUBLISHER: Zhongshan Ophthalmic Center
DOCUMENT TYPE: Journal
LANGUAGE: English
AB: The authors studied the pathogenesis of glucocorticoid-induced ***glaucoma*** (GIG) through characterization of ***glucocorticoid*** ***receptor*** (GR) on lymphocytes in Chinese patients with GIG. By radioligand receptor binding followed by Scatchard analysis, the specific binding sites were characterized and quantitated for ***glucocorticoid*** ***receptors*** on peripheral blood lymphocytes obtained from patients with GIG and the control group. The binding sites the authors detected were as follows: 12.7 +/- 1.47 times 103 receptors per cell with a KD of 3.02 +/- 0.62 nmol/L in patients with GIG, 7.26 +/- 0.45 times 103 receptors per cell with a KD of 3.03 +/- 0.56 nmol/L in the control group. The statistical difference of receptors per cell is significant between two groups, patients with GIG having more GR binding sites, while the difference of KD is not significant. The preliminary findings suggest that patients with GIG are more sensitive to glucocorticoid and the increase of binding sites of GR may be the receptor and mol. basis of the pathogenesis of GIG.

REFERENCE COUNT: 17
REFERENCE(S): (6) Benezra, D, Am J Ophthalmol 1976, V82, P8; CAPLUS (8) Bloom, E, J Steroid Biochem 1980, V12, P175 CAPLUS (11) Evans, R, Science 1988, V240, P889 CAPLUS (12) Foon, K, Am J Ophthalmol 1977, V83, P167 CAPLUS (15) Howard, K, J Biol Chem 1990, V265, P11928 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 40 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998135472 EMBASE
TITLE: Juvenile open angle ***glaucoma***
Fine mapping of the

TIGR gene to 1q24.3-q25.2 and mutation

analysis
AUTHOR: Michels-Rautenstrauss K.G.; Mardin C.Y.; Budde W.M.; Liehr T.; Polansky J.; Nguyen T.; Timmerman V.; Van Broeckhoven C.; Naumann G.O.H.; Pfeiffer R.A.; Rautenstrauss B.W.
CORPORATE SOURCE: B.W. Rautenstrauss, Institute of Human Genetics, FAU of Erlangen-Nurnberg, Schwabachanlage 10, D-91054 Erlangen, Germany
BERNDWR@HUMGENET.UNI-ERLANGEN.DE
SOURCE: Human Genetics, (1998) 102/1 (103-106)

Refs: 15
ISSN: 0340-6717 CODEN: HUGEDQ
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology 022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
AB: Autosomal dominant juvenile open angle ***glaucoma*** (JOAG) is an early-onset form of primary open angle ***glaucoma*** (POAG), which has been linked to chromosome 1q21-q31. Recently, mutations in the trabecular meshwork inducible glucocorticoid response gene (TIGR), one of the candidate genes mapped in this region, were identified in ***glaucoma*** patients of several families. We screened for mutations of the TIGR gene in two German families with JOAG and in 100 unselected sporadic cases of POAG. In the first family we identified a Pro370Leu mutation and in the second family a Gly367Arg mutation cosegregating with the ***glaucoma*** phenotype. No pathogenic mutation was found in 100 sporadic cases but a Tyr347Tyr polymorphism was found in two patients. Furthermore, fluorescence in situ hybridization (FISH) analysis was used to map a TIGR-specific yeast artificial chromosome to 1q24.3-q25.2

L6 ANSWER 17 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998-187654 BIOSIS
DOCUMENT NUMBER: PREV199800187654
TITLE: Supplement. Efficacy and safety of inhaled corticosteroids: New developments.
AUTHOR(S): Barnes, Peter J. (1), Pedersen, Soren; Busse, William W.
CORPORATE SOURCE: (1) Dep. Thoracic Med., National Heart Lung Inst., Imperial College, Dovehouse St., London SW3 6LY
UK
SOURCE: American Journal of Respiratory and Critical Care Medicine, (March, 1998) Vol. 157, No. 3 PART 2, pp. S1-S53.

ISSN: 1073-449X
DOCUMENT TYPE: General Review
LANGUAGE: English

L6 ANSWER 18 OF 40 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1997-193257 [18]
WPIDS
DOC NO CPI: C1997-061851
TITLE: New 11-(substit phenyl) oestra-4,9-diene derivs. - having anti-glucocorticoid activity used to treat e.g. Cushing syndrome, diabetes, ***glaucoma***, sleep disturbances, depression or atherosclerosis.
DERWENT CLASS: B01
INVENTOR(S): GEBHARD, R
PATENT ASSIGNEE(S): (ALKU) AKZO NOBEL

NV
COUNTRY COUNT: 32
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
AU 9662119	A	19970220	(199718)*	22	
EP 763541	A1	19970319	(199718)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI					
LU MC NL PT SE					
NO 9603427	A	19970218	(199719)		
ZA 9606555	A	19970430	(199723)	19	
CA 2182771	A	19970218	(199725)		
CZ 9602386	A3	19970514	(199726)		
JP 09104696	A	19970422	(199726)	9	
NZ 299181	A	19970922	(199745)		
HU 9602269	A2	19970428	(199801)		
KR 97010784	A	19970327	(199814)		
MX 9603476	A1	19970701	(199827)		
BR 9603429	A	19980512	(199828)		
SG 52834	A1	19980928	(199904)		
EP 763541	B1	19990728	(199934)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI					
LU MC NL PT SE					
DE 69603425	E	19990902	(199942)		
NO 306257	B1	19991011	(199949)		
AU 711369	B	19991014	(200001)		
ES 2137625	T3	19991216	(200006)		
US 6011025	A	20000104	(200008)		
RU 2135514	C1	19990827	(200033)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION DATE
AU 9662119	A	AU 1996-62119
19960816		
EP 763541	A1	EP 1996-202273
19960813		
NO 9603427	A	NO 1996-3427
19960816		
ZA 9606555	A	ZA 1996-6555
19960801		
CA 2182771	A	CA 1996-2182771
19960806		
CZ 9602386	A3	CZ 1996-2386
19960813		
JP 09104696	A	JP 1996-212824
19960812		
NZ 299181	A	NZ 1996-299181
19960815		
HU 9602269	A2	HU 1996-2269
19960816		
KR 97010784	A	KR 1996-33671
19960814		
MX 9603476	A1	MX 1996-3476
19960816		
BR 9603429	A	BR 1996-3429
19960814		
SG 52834	A1	SG 1996-10458
19960814		
EP 763541	B1	EP 1996-202273
19960813		
DE 69603425	E	DE 1996-603425
19960813		
NO 306257	B1	EP 1996-202273 19960813 NO 1996-3427
19960816		
AU 711369	B	AU 1996-62119
19960816		
ES 2137625	T3	EP 1996-202273
19960813		
US 6011025	A	Cont of US 1996-696081
19960813		
US 1997-935360		19970922
RU 2135514	C1	RU 1996-115774
19960816		

FILING DETAILS

PATENT NO	KIND	PATENT NO
DE 69603425	E Based on	EP 763541
NO 306257	B1 Previous Publ.	NO 9603427
AU 711369	B Previous Publ.	AU 9662119
ES 2137625	T3 Based on	EP 763541

PRIORITY APPLN INFO EP 1995-202229

19950817

AN 1997-193257 [18] WPI DS

AB AU 9662119 A UPAB 19970502

11-(substit. phenyl) oesta-4,9-diene derivs. of

formula (I) are new. A = a

residue of a 5 or 6-membered ring contg. 2

heteroatoms which are not

connected to each other and are selected from O or

S, and the ring is opt.

substit. by one or more halo atoms, or the residue of

a 5 or 6-membered

ring where no C=C double bonds are present and the

ring contains one

heteroatom O or S and the heteroatom is connected

to the phenyl gp. at

the position marked with the asterisk, and the ring is

opt. substit. by one

or more halo atoms; R1 = H or 1-oxo(1-4C alkyl);

R2 = H, 1-8C alkyl, halo

or CF3, X = (H,OH), O or NOH; the dotted line

represents a double or

triple bond.

USE - (I) show high ***glucocorticoid***

receptor

binding affinity and have high in vivo

anti-glucocorticoid activity. They

can be used in the treatment and/or prophylaxis of

glucocorticoid-

dependent diseases e.g. Cushing syndrome, diabetes,

glaucoma,

sleep disturbances, depression, anxiety,

atherosclerosis, hypertension,

adiposity, osteoporosis and withdrawal symptoms

from narcotics and their

mixts

ADVANTAGE - (I) lack appreciable affinity for

mineralocorticoid,

progesterone, oestrogen and androgen receptors,

indicating a clean

side-effect profile

Dwg 0/0

L6 ANSWER 19 OF 40 EMBASE COPYRIGHT

2000 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 97344241 EMBASE

DOCUMENT NUMBER: 1997344241

TITLE: Recurrent mutations in a single exon

encoding the

evolutionarily conserved

olfactomedin-homology domain of

TIGR in familial open-angle

glaucoma

AUTHOR: Adam M.F.; Belmouden A.; Binisti

P.; Brezan A.P.; Valtot

F.; Bechettoille A.; Dascotte J.-C.; Copin

B.; Gomez L.;

Chaventre A.; Bach J.-F.; Garchon H.-J.

CORPORATE SOURCE: H.-J. Garchon, INSERM

U25, Hôpital Necker, 161 rue de

Sevres, 75743 Paris cedex 15, France.

garchon@necker.fr

SOURCE: Human Molecular Genetics, (1997)

6/12 (2091-2097).

Refs. 23

ISSN 0964-6906 CODEN: HMGEES

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 012 Ophthalmology

022 Human Genetics

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Primary open-angle ***glaucoma*** (POAG)

is a highly prevalent cause

of irreversible blindness which associates cupping of

the optic disc and

alteration of the visual field, elevation of intraocular

pressure being a

major risk factor. Provided diagnosis is made at an

early stage,

treatments are available to prevent visual

impairment. A locus, GLC1A, has

been mapped on chromosome 1q23-q25 in several

families affected with

juvenile-onset POAG (JOAG) and also in some

families affected with

juvenile and middle-age onset POAG. Recently,

three mutations of the TIGR

(Trabecular meshwork-Induced Glucocorticoid

Response) gene were shown to

be responsible for the disease in several American

families and in

unrelated POAG patients. We now describe five new

mutations in eight

French families. All mutations known to date appear

to concentrate in the

evolutionarily conserved C-terminal domain of

TIGR which bears homology to

frog olfactomedin, an extracellular matrix

glycoprotein of the olfactory

epithelium, to rat and human neuronal

olfactomedin-related proteins and to

FLIC3 2, a protein from *Caenorhabditis elegans*

Moreover, this conserved

domain of TIGR is encoded by a single exon to

which mutation screening

could be limited. Surprisingly, the TIGR message,

which is abundantly

transcribed in the trabecular meshwork and also in

the ciliary body and

the sclera, is not expressed in the optic nerve whose

degeneration is,

however, the primary lesion of POAG.

L6 ANSWER 20 OF 40 EMBASE COPYRIGHT

2000 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 97288657 EMBASE

DOCUMENT NUMBER: 1997288657

TITLE: Recent advances in molecular genetics

of ***glaucomas***

AUTHOR: Sarfarazi M.

CORPORATE SOURCE: M. Sarfarazi, Surgical

Research Center, Department of

Surgery, Univ. Connecticut Health Center,

Farmington, CT

06030-1110, United States.

msarfaraz@cortex.uconn.edu

SOURCE: Human Molecular Genetics, (1997)

6/10 REV. ISS

(1667-1677)

Refs. 93

ISSN: 0964-6906 CODEN: HMGEES

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 012 Ophthalmology

022 Human Genetics

LANGUAGE: English

SUMMARY LANGUAGE: English

AB ***Glaucomas*** are a heterogeneous group of

eye conditions with

manifestation from as early as birth to very late age

of onset in life,

The primary type of these conditions affecting

children and juveniles are

less frequent, but the prevalence of

glaucomas affecting older

people of Jtoreq. 70 years progressively rises to

apprx. 5%. The

molecular genetics of three types of

glaucoma have been the

subject of investigation in the last few years. As a

result, two loci

(GLC3A and GLC3B) have been identified for

primary congenital

glaucoma, one locus (GLC1A) for

juvenile-onset primary open angle

glaucoma and a further two loci (GLC1B

and GLC1C) for late-onset

chronic open angle ***glaucoma***. Early this

year, the first set of

mutations was described in the CYP11B1

(Cytochrome P45011B1) and TIGR

(Trabecular meshwork Inducible Glucocorticoid

Response Protein) genes for

the GLC3A and GLC1A-linked families,

respectively. The mapping of

different types of ***glaucoma*** and mutation

identification in these

two genes are the focus of this review

L6 ANSWER 21 OF 40 MEDLINE

DUPLICATE 4

ACCESSION NUMBER: 97315957 MEDLINE

DOCUMENT NUMBER: 97315957

TITLE: PCR-SSCP analysis of the

glucocorticoid-responsive element

of the atrial natriuretic peptide gene in

familial primary

open-angle ***glaucoma***

AUTHOR: Richardson K.A., Tunney T.J., Clark C.

V.

CORPORATE SOURCE: University Department of

Medicine, Greenslopes Private

Hospital, Brisbane, Queensland, Australia.

SOURCE: CLINICAL AND

EXPERIMENTAL PHARMACOLOGY AND

PHYSIOLOGY,

(1997 Jun) 24 (6) 427-9

Journal code: DD8. ISSN: 0305-1870

PUB. COUNTRY: Australia

Journal; Article, (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199709

ENTRY WEEK: 19970904

AB 1. Familial primary open-angle ***glaucoma***

(POAG) is a

heterogeneous disease of unknown aetiology and the

elucidation of the

underlying genetic mechanisms contributing to

phenotypic expression will

be essential if earlier diagnosis of at-risk individuals

and more specific

medical treatment can be achieved. In a significant

percentage of patients

with POAG, intraocular pressure increases in

response to topical ocular

glucocorticoids. 2. Atrial natriuretic peptide (ANP)

assists in the

regulation of intraocular pressure levels and binding

of the

glucocorticoid ***receptor*** dimer to

the

glucocorticoid-responsive element in intron 2 of the

ANP gene has been

shown to increase ANP mRNA levels in vitro. We

amplified and examined this

sequence in the ANP gene by PCR-SSCP analysis in

100 patients with

familial POAG and in 60 normal control subjects.

No base alterations in

the amplified product were found. 3. Thus, the

present study found no

evidence for an alteration in the sequence of the

glucocorticoid-

responsive element of the ANP gene that could alter

ANP gene transcription

in patients with familial POAG. The mechanism

responsible for the increase

in intraocular pressure levels in response to

glucocorticoids is most

likely independent of the glucocorticoid-responsive

element in the ANP

gene.

L6 ANSWER 22 OF 40 SCISEARCH COPYRIGHT

2000 ISI (R)

ACCESSION NUMBER: 96:286937 SCISEARCH

THE GENUINE ARTICLE: UD853

TITLE: INHIBITION OF

DEXAMETHASONE-INDUCED CYTOSKELETAL

CHANGES

IN CULTURED HUMAN

TRABECULAR MESHWORK CELLS BY

TETRAHYDROCORTISOL

AUTHOR: CLARK A.F. (Reprint), LANE D.

WILSON K., MCGAGNAN S.T.

MCCARTNEY M.D.

CORPORATE SOURCE: ALCON LABS INC.

GLAUCOMA RES R241, 6201 S FREEWAY, FT

WORTH, TX, 76134 (Reprint)

COUNTRY OF AUTHOR: USA

SOURCE: INVESTIGATIVE

OPHTHALMOLOGY & VISUAL SCIENCE, (APR

1996)

Vol 37, No. 5, pp. 805-813

ISSN: 0146-0404

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: ENGLISH

REFERENCE COUNT: 47

*ABSTRACT IS AVAILABLE IN THE

ALL AND IALL FORMATS*

AB Purpose, To determine the cellular mechanism of action of the intraocular pressure (IOP) lowering steroid tetrahydrocortisol (THF).

Methods, Tetrahydrocortisol was evaluated for glucocorticoid antagonist activity using in vitro and in vivo assays. Systemically administered THF was evaluated for its ability to inhibit dexamethasone-induced body weight loss and systemic hypertension in rats. In vitro receptor antagonism was tested using the supernatant fraction of IM9 cells as the source of soluble ***glucocorticoid*** ***receptor*** in H-3-dexamethasone displacement binding assays. In addition, six different primary human trabecular meshwork (TM) cell lines were cultured for 0 to 14 days in the absence or presence of dexamethasone (10(-7) M) and/or THF (10(-6) to 10(-6) M). The effects of these steroids on the TM cytoskeleton were determined by epifluorescent microscopy and by transmission electron microscopy.

Results, Tetrahydrocortisol was unable to inhibit the dexamethasone (DEX)-induced systemic hypertension and decrease in body mass in rats and was unable to displace H-3-DEX from the soluble human ***glucocorticoid*** ***receptor***.

However, THF inhibited the DEX-induced formation of cross-linked actin networks in cultured human TM cells in a progressive and dose-dependent manner (IC50 = 5.7 x 10(-7) M).

Dexamethasone caused changes in the TM cell microtubules that were reversed partially by concomitant treatment with THF. Tetrahydrocortisol alone appeared to increase microfilament bundling in TM cells.

Conclusions, Tetrahydrocortisol was not a glucocorticoid antagonist at the level of the classical ***glucocorticoid*** ***receptor*** and did not appear to antagonize systemically mediated glucocorticoid activity in the rat. Tetrahydrocortisol inhibited DEX-induced changes in the TM microfilaments and microtubules. These results may explain partially the IOP lowering activity of THF because glucocorticoid-mediated changes in the TM cytoskeleton have been proposed to be involved in the generation of ocular hypertension.

L6 ANSWER 23 OF 40 MEDLINE
DUPLICATE 5
ACCESSION NUMBER: 96330663 MEDLINE
DOCUMENT NUMBER: 96330663
TITLE: Fluticasone propionate: topical or systemic effects?
AUTHOR: Howland W C 3rd
CORPORATE SOURCE: Healthquest Research, Austin, Texas 78759, USA
SOURCE: CLINICAL AND EXPERIMENTAL ALLERGY, (1996 May) 26 Suppl 3

18-22
Journal code CEB ISSN 0954-7894
PUB COUNTRY: ENGLAND: United Kingdom (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal, Article, (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY WEEK: 19970304
AB Intranasal corticosteroids have been shown to be more effective than oral

antihistamines for the treatment of seasonal allergic rhinitis. However, there are some who question whether intranasally administered corticosteroids should be used due to potential systemic effects.

Fluticasone propionate, a potent corticosteroid with high specificity for the ***glucocorticoid*** ***receptor***, is available as an aqueous nasal spray for the treatment of allergic rhinitis. To determine whether the efficacy of fluticasone propionate aqueous nasal spray (FPANS) was due to direct topical effects on the nasal mucosa or to indirect systemic effects following absorption from the nasal mucosa or from the swallowed portion of an intranasal dose, FPANS 200 micrograms once daily was compared with oral fluticasone propionate 5 mg or 10 mg once daily or placebo for 2 weeks in patients with seasonal allergic rhinitis. These oral dosages were chosen to yield low but consistent plasma fluticasone propionate concentrations. Both clinician- and patient-rated scores for nasal obstruction, rhinorrhoea, sneezing, and nasal itching were significantly lower in the intranasal fluticasone propionate group compared with both oral fluticasone propionate groups. A separate placebo-controlled study was conducted in patients with perennial rhinitis to determine if administration of FPANS 200 micrograms once daily for 1 year was associated with adverse systemic effects. At the 1-year assessment, there were no significant effects on bone mineral density or on biochemical markers of bone turnover. Similarly, there was no evidence of posterior subcapsular cataracts nor of ***glaucoma***. Furthermore, there were no significant effects on hypothalamic-pituitary-adrenal axis function as assessed by plasma cortisol and 24-h urinary cortisol response to the 6-h cosyntropin stimulation test. These data confirm that the efficacy of FPANS for the treatment of allergic rhinitis results from direct topical effects, thus reducing the likelihood of adverse systemic effects.

Fluticasone propionate, a potent corticosteroid with high specificity for the ***glucocorticoid*** ***receptor***, is available as an aqueous nasal spray for the treatment of allergic rhinitis. To determine whether the efficacy of fluticasone propionate aqueous nasal spray (FPANS) was due to direct topical effects on the nasal mucosa or to indirect systemic effects following absorption from the nasal mucosa or from the swallowed portion of an intranasal dose, FPANS 200 micrograms once daily was compared with oral fluticasone propionate 5 mg or 10 mg once daily or placebo for 2 weeks in patients with seasonal allergic rhinitis. These oral dosages were chosen to yield low but consistent plasma fluticasone propionate concentrations. Both clinician- and patient-rated scores for nasal obstruction, rhinorrhoea, sneezing, and nasal itching were significantly lower in the intranasal fluticasone propionate group compared with both oral fluticasone propionate groups. A separate placebo-controlled study was conducted in patients with perennial rhinitis to determine if administration of FPANS 200 micrograms once daily for 1 year was associated with adverse systemic effects. At the 1-year assessment, there were no significant effects on bone mineral density or on biochemical markers of bone turnover. Similarly, there was no evidence of posterior subcapsular cataracts nor of ***glaucoma***. Furthermore, there were no significant effects on hypothalamic-pituitary-adrenal axis function as assessed by plasma cortisol and 24-h urinary cortisol response to the 6-h cosyntropin stimulation test. These data confirm that the efficacy of FPANS for the treatment of allergic rhinitis results from direct topical effects, thus reducing the likelihood of adverse systemic effects.

L6 ANSWER 24 OF 40 EMBASE COPYRIGHT
2000 ELSEVIER SCI B V
ACCESSION NUMBER: 96153145 EMBASE
DOCUMENT NUMBER: 1996153145
TITLE: Fluticasone propionate: Topical or systemic effects?
AUTHOR: Howland III W C
CORPORATE SOURCE: Healthquest Research, 3807 Spicewood Springs Road, Austin, TX 78759, United States
SOURCE: Clinical and Experimental Allergy, Supplement, (1996) 26/3 (18-22)
ISSN: 0960-2178 CODEN: CLASEN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal, Conference Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
011 Otorhinolaryngology

LANGUAGE: English
SUMMARY LANGUAGE: English
AB Intranasal corticosteroids have been shown to be more effective than oral antihistamines for the treatment of seasonal allergic rhinitis. However, there are some who question whether intranasally administered corticosteroids should be used due to potential systemic effects.

Fluticasone propionate, a potent corticosteroid with high specificity for the ***glucocorticoid*** ***receptor***, is available as an aqueous nasal spray for the treatment of allergic rhinitis. To determine whether the efficacy of fluticasone propionate aqueous nasal spray (FPANS) was due to direct topical effects on the nasal mucosa or to indirect systemic effects following absorption from the nasal mucosa or from the swallowed portion of an intranasal dose, FPANS 200 mu g once daily was compared with oral fluticasone propionate 5 mg or 10 mg once daily or placebo for 2 weeks in patients with seasonal allergic rhinitis. These oral dosages were chosen to yield low but consistent plasma fluticasone propionate concentrations. Both clinician- and patient-rated scores for nasal obstruction, rhinorrhoea, sneezing, and nasal itching were significantly lower in the intranasal fluticasone propionate group compared with both oral fluticasone propionate groups. A separate placebo-controlled study was conducted in patients with perennial rhinitis to determine if administration of FPANS 200 mu g once daily for 1 year was associated with adverse systemic effects. At the 1-year assessment, there were no significant effects on bone mineral density or on biochemical markers of bone turnover. Similarly, there was no evidence of posterior subcapsular cataracts nor of ***glaucoma***. Furthermore, there were no significant effects on hypothalamic-pituitary-adrenal axis function as assessed by plasma cortisol and 24-h urinary cortisol response to the 6-h cosyntropin stimulation test. These data confirm that the efficacy of FPANS for the treatment of allergic rhinitis results from direct topical effects, thus reducing the likelihood of adverse systemic effects.

L6 ANSWER 25 OF 40 EMBASE COPYRIGHT
2000 ELSEVIER SCI B V
ACCESSION NUMBER: 95173327 EMBASE
DOCUMENT NUMBER: 1995173327
TITLE: Ophthalmic corticosteroids and steroid ***glaucoma*** mechanisms.
AUTHOR: Polansky J R., Fauss D J., Nguyen T D.
CORPORATE SOURCE: Department of Ophthalmology, UCSF School of Medicine, San Francisco, CA 94143-0730, United States
SOURCE: Ophthalmology Clinics of North America, (1995) 8/2 (215-228+ix)
ISSN: 0896-1549 CODEN: OCNAF2
COUNTRY: United States
DOCUMENT TYPE: Journal, General Review
FILE SEGMENT: 012 Ophthalmology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Studies of basic pharmacologic parameters, including

glucocorticoid ***receptor*** -binding, susceptibility to metabolism, and active drug levels in the aqueous humor by radio-receptor assay have helped to define potentially important differences in the ophthalmic corticosteroids available for clinical use. Information gained by these evaluations has aided in the interpretation of prior in vivo clinical and experimental animal data with regards to

both anti-inflammatory effects and the propensity of these drugs to raise intraocular pressure (IOP). Potentially relevant new leads to evaluate the IOP side-effects of corticosteroids have also been developed by evaluating dexamethasone regulation of specific protein synthesis and cell division in human trabecular meshwork endothelial cells, as the probable 'target cell' for the observed reduction in outflow facility.

L6 ANSWER 26 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1995-272333 BIOSIS
DOCUMENT NUMBER: PREV199598286633
TITLE: Clinical uses of antiprostaglandins
AUTHOR(S): Van Look, Paul F. A. (1); Von Herten, Helena
CORPORATE SOURCE: (1) Special Programme Res., Dev. Res. Training Human Reproduction, World Health Organization, Avenue Appia, 1211 Geneva 27 Switzerland

SOURCE: Human Reproduction Update, (1995) Vol. 1, No. 1, pp. 19-34
ISSN: 1355-4786

DOCUMENT TYPE: General Review
LANGUAGE: English

AB Antiprostaglandins, which block the action of progesterone at the cellular level through binding to the progesterone receptor, are proving to be one of the most significant developments in endocrinology in recent years.

Several hundreds of such compounds have been synthesized, but only a few of them have been evaluated to any significant extent in biological screening models and, to our knowledge, only three compounds, namely mifepristone, iloprostone (ZK 98.734) and onapristone (ZK 98.299) have been given to humans. Most of the clinical research to date has focused on the use of mifepristone given in combination with prostaglandin for termination of early pregnancy, an indication for which the compound is being used routinely in four countries so far, i.e. China, France, the UK and Sweden. The gynaecological and obstetrical applications in which antiprostaglandins have been shown to be of value to date include ripening of the pregnant cervix prior to pregnancy termination, sensitization of the uterus to prostaglandins in second-trimester abortion, and induction of labour. Available data suggest that antiprostaglandins have no place in the conservative treatment of ectopic pregnancy or in the treatment of premenstrual tension. In fertility regulation, the sequential combination regimen of mifepristone plus prostaglandin as used for inducing abortion has proved to be effective also for menses induction and can be expected to be an efficacious once-a-month contraceptive. Mifepristone alone, without adjuvant prostaglandin, has yielded promising results as an anti-implantation agent and in emergency contraception. Other potential uses include once-a-week contraception, ovulation inhibition (in a sequential regimen with a progestogen), and as a daily mini-pill. Mifepristone, and other antiprostaglandins for which biological data have been reported also bind to the cellular receptors for glucocorticoid hormones and, consequently, possess antiglucocorticoid in addition to their antiprostaglandin activity. Because of this antiglucocorticoid

effect, mifepristone has been employed successfully in the palliative treatment of hypercortisolism due to Cushing's syndrome, and its use has been proposed for treating certain forms of depression and of ***glaucoma***, and in wound healing. However, for scientific and practical reasons, it would be preferable if molecules were developed that have only the antiprostaglandin or the antiglucocorticoid activity rather than both.

L6 ANSWER 27 OF 40 MEDLINE
DUPLICATE 6
ACCESSION NUMBER: 94131755 MEDLINE
DOCUMENT NUMBER: 94131755
TITLE: Glucocorticoid-induced formation of cross-linked actin networks in cultured human trabecular meshwork cells.
AUTHOR: Clark A F; Wilson K; McCartney M D; Miggans S T; Kunkle M; Howe W
CORPORATE SOURCE: Alcon Laboratories, Inc., Fort Worth, Texas 76134.
SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1994 Jan)

35 (1) 281-94
Journal code: GWI. ISSN: 0146-0404
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199405

AB PURPOSE: To determine the effects of glucocorticoid treatment on the microfilament structure of cultured human trabecular meshwork cells.

Topical or systemic administration of glucocorticoids can lead to the development of ocular hypertension and to the development of vision loss, which is clinically similar to primary open angle ***glaucoma***.

However, the mechanism(s) by which glucocorticoids cause ocular hypertension is not well defined. Alterations in the trabecular meshwork, the site of drainage of aqueous humor from the eye, have been linked to the development of ocular hypertension.

METHODS: Human trabecular meshwork cells were cultured in the presence and absence of glucocorticoids for 0

to 21 days. The microfilament organization of the cultured trabecular meshwork cells was examined by epifluorescent and transmission electron microscopy.

RESULTS: Glucocorticoids caused a progressive change in the organization of microfilaments in the trabecular meshwork cells, but not in other cultured ocular cells. By fluorescence microscopic analysis, the actin stress fibers found in control trabecular meshwork cells were reorganized on treatment with glucocorticoids into cross-linked actin

networks that resembled geodesic-dome-like polygonal lattices. The

cross-linked actin networks were reversible on withdrawal of the glucocorticoid treatment. Dose-response data for dexamethasone, relative ranking of activity with glucocorticoid potency, and partial inhibition

with glucocorticoid antagonists all suggest the involvement of the trabecular meshwork ***glucocorticoid*** ***receptor*** in

cross-linked actin network formation. The reorganization of the trabecular meshwork cytoskeleton alters cell function because glucocorticoid treatment of cultured trabecular meshwork cells also

inhibited trabecular meshwork cell migration and proliferation.
CONCLUSION: The steroid-induced alteration in trabecular meshwork cytoskeleton may be an important factor in the development of steroid-induced ocular hypertension and may play a role in the ocular hypertension associated with primary open angle ***glaucoma***.

L6 ANSWER 28 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1992-330593 BIOSIS
DOCUMENT NUMBER: BA94-32434
TITLE: MIFEPRISTONE BLOCKS SPECIFIC ***GLUCOCORTICOID*** ***RECEPTOR*** BINDING IN RABBIT IRIS-CILIARY BODY.
AUTHOR(S): MUNDEN P M; SCHMIDT T J
CORPORATE SOURCE: DEP. OPHTHALMOL., UNIV. IOWA HOSP. CLIN., IOWA CITY, IOWA 52242
SOURCE: ARCH. OPHTHALMOL., (1992) 110 (5), 703-705

CODEN: AROPAW. ISSN: 0003-9950.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Mifepristone is a specific ***glucocorticoid*** ***receptor***

antagonist that has been shown to lower intraocular pressure modestly when applied topically to rabbit eyes. We evaluated the ability of mifepristone

to block specific in vitro ***glucocorticoid*** ***receptor***

binding to the labeled agonist triamcinolone acetonide in cytosol isolated from rabbit iris-ciliary body tissue. A 500-fold molar excess of nonradioactive mifepristone completely blocked specific binding of

triamcinolone acetonide to ***glucocorticoid*** ***receptors***

in the iris-ciliary body cytosol. Additionally, specific binding was blocked in a dose-dependent fashion over a range of 0.005-fold to 500-fold

molar excess of mifepristone. Mifepristone's effect on intraocular pressure may be due to its ability to antagonize ***glucocorticoid***

receptor-mediated effects in ocular tissues.

L6 ANSWER 29 OF 40 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92350940 EMBASE
DOCUMENT NUMBER: 1992350940
TITLE: Role of receptors in the trabecular meshwork of the eye as targeted to the development of antiglaucoma therapy.
AUTHOR: Tripathi R.C., Yang C., Tripathi B.J., Borisuth N.S.C.
CORPORATE SOURCE: University of Chicago, Visual Sciences Center, 939 East 57th Street, Chicago, IL 60637, United States

SOURCE: Drug Development Research, (1992) 27/3 (191-228).

ISSN: 0272-4391 CODEN: DDREDK
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 002 Physiology
012 Ophthalmology
037 Drug Literature Index

LANGUAGE: English
SUMMARY LANGUAGE: English
AB The major pathway for the outflow of aqueous humor from the anterior chamber of the eye is the trabecular meshwork/Schlemm's canal system. The meshwork is composed of connective tissue beams that are ensheathed by trabecular cells, these cells derive their nutrition from the aqueous humor and thus are uniquely susceptible to

morphologic and biochemical regulation by bioactive substances that are present or released in this fluid and to pharmacologic agents that are targeted to act on the tissue.

The receptors that have been detected on trabecular cells include those for growth modulatory peptides (bFGF, TGF- β 1, transferrin, IGF-1, and EGF), epinephrine, dopamine, glucocorticoids, benzodiazepines, prostanoids, biogenic amines, the Fc portion of IgGs, and probably those for molecules of the extracellular matrix (integrins).

Selective up- or down-regulation of the receptors on the trabecular cells would facilitate an effective control of the intraocular pressure in diseased conditions of the eye. We discuss the prospects and hurdles in the utilization of receptor targeting as a therapeutic modality for trabecular cell regeneration in ***glaucoma*** as well as for pharmacologic trabeculectomy and as a treatment for hypotony after ***glaucoma*** filtration surgery. We believe that regulation of receptor expression is a novel method for the development of new antiglaucoma agents and for minimizing the side effects of drugs that are administered topically and systemically for the control of the intraocular pressure.

L6 ANSWER 30 OF 40 MEDLINE
 DUPLICATE 7
 ACCESSION NUMBER: 91201034 MEDLINE
 DOCUMENT NUMBER: 91201034
 TITLE: Increased plasma noncortisol glucocorticoid activity in open-angle ***glaucoma*** [published erratum appears in Invest Ophthalmol Vis Sci 1991 Jul;32(8) 2440]
 AUTHOR: McCarty G R, Schwartz B
 CORPORATE SOURCE: Department of Ophthalmology, New England Medical Centre Hospitals, Boston, Massachusetts 02111..
 CONTRACT NUMBER: EY00024 (NEI) EY07045 (NEI)
 SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1991 Apr) 32 (5) 1600-8
 Journal code: GWL ISSN: 0146-0404.
 PUB. COUNTRY: United States
 Journal, Article, (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199107
 AB Total biologic plasma glucocorticoid activity of normal, ocular hypertensive, and open-angle ***glaucoma*** patients was compared using a ***glucocorticoid*** ***receptor***-based competitive binding assay. Multiple linear-regression analysis was used to adjust for the effects of significant ocular and nonocular variables, including therapy for ***glaucoma***. The ***glaucoma*** patients had significantly greater plasma glucocorticoid activities than did normal subjects. A comparison of receptor-based assay values to values obtained with a cortisol radioimmunoassay showed that significant amounts of biologic glucocorticoid activity in the plasma of the ***glaucoma*** patients could not be explained by cortisol alone. In the normal and ocular hypertensive groups, however, virtually all of the plasma glucocorticoid activity could be accounted for by cortisol. These results

suggest that in open-angle ***glaucoma*** patients, noncortisol glucocorticoids are responsible for elevating biologic plasma glucocorticoid activity. Thus, open-angle ***glaucoma*** may be associated with a disturbance of the hypothalamic-pituitary-adrenal axis that produces increased plasma levels of both cortisol and other noncortisol glucocorticoids.

L6 ANSWER 31 OF 40 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1990-022375 [03]
 WPIDS
 DOC NO: CPI C1990-009886
 TITLE: New 11-aryl-19-nor-progesterone derivs. - useful as progestational or anti-progestational agents and/or anti-glucocorticoid agents.
 DERWENT CLASS B01
 INVENTOR(S) COOK, C E, LEE, Y;
 RECTOR, D; REEL, J R; WANI, M C; COOK, E, REEL, J
 PATENT ASSIGNEE(S): (RETR-N) RES TRIANGLE INST
 COUNTRY COUNT: 18
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8912448	A	19891228 (199003)*	EN	50	
RW: AT BE CH DE FR GB IT LU NL SE W: AU DK JP KR NO					
AU 8938506	A	19900112 (199013)			
US 4954490	A	19900904 (199038)			
EP 422100	A	19910417 (199116)			
R: AT BE CH DE FR GB IT LI LU NL SE					
NO 9005546	A	19901221 (199116)			
DK 9003053	A	19901221 (199131)			
US 5073548	A	19911217 (199202)			
JP 03505582	W	19911205 (199204)			
AU 635211	B	19930318 (199318)			
EP 422100	A4	19940427 (199530)			
NO 178264	B	19951113 (199550)			
EP 422100	B1	19970312 (199715)	EN	28	
R: AT BE CH DE FR GB IT LI LU NL SE					
CA 1338906	C	19970211 (199718)			
DE 68927861	E	19970417 (199721)			
JP 2953725	B2	19990927 (199945)	19		
KR 161975	B1	19981116 (200030)			

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION DATE
WO 8912448	A	WO 1989-US2706
19890623		
US 4954490	A	US 1988-210503
19880623		
EP 422100	A	EP 1989-907924
19890623		
US 5073548	A	US 1990-504129
19900403		
JP 03505582	W	JP 1989-507392
19890623		
AU 635211	B	AU 1989-38506
19890623		
EP 422100	A4	EP 1989-907924
NO 178264	B	WO 1989-US2706
19890623		
EP 422100	B1	NO 1990-5546 19901221 EP 1989-907924
19890623		
CA 1338906	C	WO 1989-US2706 19890623 CA 1989-603686
19890622		
DE 68927861	E	DE 1989-627861
19890623		
EP 1989-907924		19890623
WO 1989-US2706		19890623
JP 1989-507392		
WO 1989-US2706		19890623
KR 161975	B1	KR 1990-700406

19900222

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 635211	B Previous Publ	AU 8938506
Based on WO 8912448		
NO 178264	B Previous Publ	NO 9005546
EP 422100	B1 Based on	WO 8912448
DE 68927861	E Based on	EP 422100
Based on WO 8912448		
JP 2953725	B2 Previous Publ	JP 03505582
Based on WO 8912448		

PRIORITY APPLN. INFO. US 1988-210503 19880623
 AN 1990-022375 [03] WPIDS
 AB WO 8912448 A UPAB: 19930928
 Beta-Aryl-19-norprogesterones of formula (I) are new. Where R1 = H, 1-4C alkyl, 2-4C alkenyl, 2-4C alkynyl, OH, OCOMe or OCOR5; R5 = 2-8C alkyl, 2-8C alkenyl, 2-8C alkynyl or aryl; R2 = H; R3 = H, 1-4C alkyl, 2-4C alkenyl or 2-4C alkynyl. R4 = H, Me, F or Cl; R6 = H, NMe2, OMe, COMe, SMe, SOMe or SO2Me; X = 0 or NOME; or R1 + R2 is a bond; or R1 + R3 is CH2 or N = NCH2, in which case R2 = H, or R2 + R3 is CH2.

USE - (I) have progestational or antiprogesterone activity and/or antiglucocorticoid activity. They may be useful as antifertility agents and in the treatment of Cushing's syndrome, ***glaucoma***, endometriosis, premenstrual syndrome and cancer, and for oestrus regulation in animals.

0/0
 ABEQ US 4954490 A UPAB: 19930928
 11beta-aryl-19-norprogesterone of formula (I) is new. R1 is OC(O)CH3, OC(O)R5, where R5 is 2-8C-alkyl, -alkenyl, or -alkynyl or aryl; R2 is H; R3 is H, 1-4C alkyl, 2-4C-alkenyl or -alkynyl; R4 is H, Me, F, Cl; R6 is H, Me2N, MeO, Ac, MeS, MeSO, MeSO2; X is O, NOME. Esp. cps. include 17alpha-acetoxy-6alpha-methyl-11beta-(4-N,N-dimethylaminophenyl)-19-norpregna-4,9-diene-3,20-dione. USE - These cps. bind strongly to progesterone and ***glucocorticoid*** ***receptors*** with progestational, anti-progestational and anti-glucocorticoid activity, used in treatment of cancer, and Cushing's syndrome and ***glaucoma***. Unit dose 0.1 mg-2g.

ABEQ US 5073548 A UPAB: 19930928
 Beta-Aryl-19-norprogesterones of formula (I) are new. Where R1 = H, 1-4C alkyl, 2-4C alkenyl, 2-4C alkynyl, OH, OCOMe or OCOR5; R5 = 2-8C alkyl, 2-8C alkenyl, 2-8C alkynyl or aryl; R2 = H; R3 = H, 1-4C alkyl, 2-4C alkenyl or 2-4C alkynyl; R4 = H, Me, F or Cl; R6 = H, NMe2, OMe, COMe, SMe, SOMe or SO2Me; X = 0 or NOME; or R1 + R2 is a bond; or R1 + R3 is CH2 or N = NCH2, in which case R2 = H, or R2 + R3 is CH2.

USE - (I) have progestational or antiprogesterone activity and/or antiglucocorticoid activity. They may be useful as antifertility agents and in the treatment of Cushing's syndrome, ***glaucoma***, endometriosis, premenstrual syndrome and cancer, and for oestrus regulation in animals.

ABEQ EP 422100 B UPAB: 19970410
 An 11beta-phenyl-19-norprogesterone of the formula (I), wherein (i) (1) R1 is OC(OH)CH3 or OC(O)R5, wherein R5 is C2-8 alkyl, C2-8 alkenyl, C2-8

alkenyl or aryl, R2 is H, R3 is H, C1-4 alkyl, C2-4 alkenyl or C2-4 alkenyl, R4 is H, CH3, F or Cl, R6 is H, (CH3)2N, CH3O, CH3CO, CH3S, CH3SO, CH3SO2, and X is O or NOCH3, or (i) (2) R1 is C2-4 alkenyl or C2-4 alkenyl, R2 is H, R3 is H, C1-4 alkyl, C2-4 alkenyl or C2-4 alkenyl, R4 is H, CH3, F or Cl, R6 is H, (CH3)2N, CH3O, CH3CO, CH3S, CH3SO, CH3SO2, and X is O or NOCH3, or (i) (3) R1 is C2-4 alkyl, R2 is H, R3 is H, C1-4 alkyl, C2-4 alkenyl or C2-4 alkenyl, R4 is H, CH3, F or Cl, R6 is H, (CH3)2N, CH3O, CH3CO, CH3S, CH3SO, CH3SO2, and X is O or NOCH3, or (ii) R1 and R2 taken together are a carbon-carbon bond, R3 is H, C1-4 alkyl, C2-4 alkenyl or C2-4 alkenyl, R4 is H, CH3, F or Cl, R6 is H, (CH3)2N, CH3O, CH3CO, CH3S, CH3SO, CH3SO2, and X is O or NOCH3, or (iii) R1 and R3 taken together are -CH2- or -N=N-CH2-, R2 is H, R4 is H, CH3, F or Cl, R6 is H, (CH3)2N, CH3O, CH3CO, CH3S, CH3SO, CH3SO2, and X is O or NOCH3, or (iv) R2 and R3 taken together are =CH2, R1 is H, C1-4 alkyl, C2-4 alkenyl or C2-4 alkenyl, R4 is H, CH3, F or Cl, R6 is H, (CH3)2N, CH3O, CH3CO, CH3S, CH3SO, CH3SO2, and X is O or NOCH3

Dwg 2/2

L6 ANSWER 32 OF 40 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1988-091693 [13]
 WPIDS
 DOC. NO. CIP: C1988-041156
 TITLE: Steroid(s) having binding affinity for ***glucocorticoid*** ***receptor***
 - are 17
 alpha-subst-d-methyl-17
 beta-hydroxy-steroid derivs.
 DERWENT CLASS: B01 C03
 INVENTOR(S): COOK, C E, REEL, J R, TALLENT, C R; WANI, M C, EDGAR, C, JERRY, R, TALLENT, C
 PATENT ASSIGNEE(S): (RETR-N) RES TRIANGLE INST
 COUNTRY COUNT: 11
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8801868	A	19880324 (198813)*	EN	45	
RW BE CH DE FR GB IT					
W: AU JP NL					
AU 8780208	A	19880407 (198827)			
US 4774236	A	19880927 (198841)		13	
US 4861763	A	19890829 (198944)		11	
CA 1327791	C	19940315 (199416)			

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION DATE
WO 8801868	A	WO 1987-US2303
19870915		
US 4774236	A	US 1986-908288
19860917		
US 4861763	A	US 1988-223873
19880725		
CA 1327791	C	CA 1987-547105
19870917		

PRIORITY APPLN. INFO: US 1986-908288
 19860917, US 1988-223873
 19880725
 AN 1988-091693 [13] WPIDS
 AB WO 8801868 A UPAB 19930923
 (1) Steroids having binding affinity for the

glucocorticoid
 receptor and possessing glucocorticoid activity and of formula (I)
 are new Either the 1(2)-bond is single and the 9(10)-bond is double and A is absent, or the 1(2)-bond is single or double, the 9(10)-bond is single and A=Me; X = ethynyl, CN, N3, SCN, OMe or Ph, R = H or 1-5C acyl, R1 = Me, R2 = (alpha H, beta OH) except when X = CN, or O, R3 = H (2) In (1) when there is 1,2-dihydro, and 4, 9(10) dihydro, then R1 may also be Et; and R2 = alpha H, together with (CH2)nR5, R5 = pyridyl, thiazolyl, NMe2, NEt2, 1-piperidinyl, 4-methyl-1-piperidinyl, OMe, C6H4R4, R4 = R5 or H, O(CH2)2NMe2, O(CH2)2NEt2, 1-3C alkoxy, halogen, 1-3C alkylthio, 1-3C alkylsulphonyl, Ph S or Ph SO, or (alpha H, beta CF3), (alpha H, beta CHF2), = CHF or = CF2 Other combinations of substituents may be present.
 USE/ADVANTAGE - (I) have glucocorticoid and antiglucocorticoid, progestational and antiprogesterational activities. Dose is 0.0001-1g/unit dose.
 /0
 ABEQ US 4774236 A UPAB: 19930923
 Glucocorticoid ***receptor*** -binding
 17-alpha-(subst-d-methyl)-17beta-hydroxy/esterified hydroxy steroids of formula (II) where Z is of partial structure (III) or (IV), are new. In these formulae X is -C=CH, CN, N3, SCN, OMe, Ph, R is Ac, propionyl, butyryl; R1 is Me; R2 is alpha-H, beta-OH or =O provided that when X is CN, R2 is O, R3 is H.
 USE - These steroids have glucocorticoid, anti-glucocorticoid, anti-glucocorticoid, progestational and anti-progestational activity depending on structure, having binding affinities to both types of receptor and are used in treatment of inflammatory and allergic conditions.
 glaucoma, stress and as contraceptive or estrogenic agents to control fertility, and as antitumour agents. Dose e.g. 0.0001-1(0.001-1)g.
 ABEQ US 4861763 A UPAB: 19930923
 New steroids with binding affinity for the progesterone receptor and having progestational activity are of formula (I) where X = CN, N3, SCN, OMe or Ph opt. subst. by 1-3C alkyl. R = H or 1-5C acyl. R1 = methyl or ethyl. R2 = alpha-H and beta-(1-3C alkyl); or alpha-H and beta-(2-4C alkenyl); or methylene, or alpha-H and beta-p-fluorophenyl; or alpha-H and beta-p-trifluoromethylphenyl; or alpha-H and beta-thienyl; and R3 = H or methyl.

L6 ANSWER 33 OF 40 MEDLINE
 DUPLICATE 8
 ACCESSION NUMBER: 85233754 MEDLINE
 DOCUMENT NUMBER: 85233754
 TITLE: Cellular sensitivity to glucocorticoids in patients with POAG. Steroid receptors and responses in cultured skin fibroblasts.
 AUTHOR: Polansky J, Palmberg P, Matulich D, Lan N, Hajek S, Hajek A, Becker B, Baxter J
 CONTRACT NUMBER: EY-01785 (NEI)
 EY-01167 (NEI)
 EY-02477 (NEI)
 +
 SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1985 Jun)
 26 (6) 805-9
 Journal code: GW1 ISSN: 0146-0404.

PUB COUNTRY: United States
 Journal, Article, (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 198510
 AB The question of a generalized hypersensitivity to corticosteroids in primary open-angle ***glaucoma*** (POAG) was investigated using cultured skin fibroblasts from patients with POAG and age-matched controls. Nuclear binding of (3H)-dexamethasone was performed to evaluate possible changes in the ***glucocorticoid*** ***receptors***.
 Cortisol effects on (3H)-thymidine uptake into the cells were investigated as a measure of the cellular sensitivity to corticosteroids. When POAG and control groups were compared, no significant differences (P less than 0.05) were found for either the number or affinity of ***glucocorticoid*** ***receptors***.
 (POAG: Kd = 6.1 +/- 1.0 nM, Rt = 94 +/- 13 sites/cell X 10(3); control: Kd = 5.5 +/- 1.6 nM, Rt = 124 +/- 20 X 10(3) sites/cell) or for cortisol effects on thymidine uptake (POAG: C50 = 83 +/- 38 nM; control: C50 = 80 +/- 34 nM).
 Use of epidermal growth factor (EGF) resulted in an increased steroid sensitivity in some cell lines, but again no differences between POAG and control groups were detected. These results suggest that a generalized cellular hypersensitivity to glucocorticoids is not intrinsic to POAG. It is possible that environmental alterations and/or endogenous factors may influence the steroid responses observed in these patients.

L6 ANSWER 34 OF 40 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 9
 ACCESSION NUMBER: 1984.62502 CAPLUS
 DOCUMENT NUMBER: 100.62502
 TITLE: Prostaglandin production by human trabecular cells:
 in vitro inhibition by dexamethasone
 AUTHOR(S): Weinreb, Robert N; Mitchell, Murray D; Polansky, Jon
 R
 CORPORATE SOURCE: Med. Cent., Univ. California, San Francisco, CA, USA
 SOURCE: Invest. Ophthalmol. Visual Sci. (1983), 24(12), 1541-5
 CODEN: IOVSDA, ISSN: 0146-0404
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Morphol. differentiated human trabecular cells produced high levels of PGE2 [363-24-6] and somewhat lower levels of PGF2 alpha. [551-11-1], and 6-keto-PGF1 alpha. [6KF1 alpha] [58962-34-8] in the presence and absence of serum. In a typical expt., the following PG levels were detected in the cell culture media after 24 h: PGE2, 225, PGF2 alpha., 33.5, 6KF1 alpha., 12.7 ng/mL in the presence of 10% fetal calf serum, and PGE2, 30.0, PGF2 alpha., 4.8, 6KF1 alpha., 3.6 ng/mL in serum-free media.
 Moderate concns. of dexamethasone (DEX) [50-02-2] decreased the levels of all 3 PGs. For PGE2 prodn., 10-8M DEX inhibited approx. 75%, and 10-7M DEX inhibited approx. 90%. The IC50 for inhibition of PG prodn. by DEX was <10 nM, thus indicating that the steroid effect probably involved high-affinity ***glucocorticoid*** ***receptors***. These findings emphasize the possibility that physiol. levels of glucocorticoids may regulate PG prodn. within the meshwork, and suggest that studies of

endogenous PG prodn by trabecular cells could provide new clues to the pathogenesis of a no. of ***glaucoma*** syndromes, including primary open-angle ***glaucoma*** and steroid ***glaucoma***

L6 ANSWER 35 OF 40 MEDLINE
DUPLICATE 10
ACCESSION NUMBER: 84017537 MEDLINE
DOCUMENT NUMBER: 84017537
TITLE: Potentiation of glucocorticoid activity by 5

beta-dihydrocortisol: its role in
glaucoma
AUTHOR: Weinstein B I; Gordon G G,
Southren A L
CONTRACT NUMBER: EY 01313 (NEI)
SOURCE: SCIENCE, (1983 Oct 14) 222
(4620) 172-3.

Journal code: UJ7 ISSN: 0036-8075
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 198401
AB 5 beta-Dihydrocortisol potentiated the threshold level (the smallest dose producing a measurable effect) of topically applied cortisol (0.02 percent) and dexamethasone (0.003 percent) in causing nuclear translocation of the cytosolic ***glucocorticoid*** ***receptor*** in rabbit iris-ciliary body tissue. 5 beta-Dihydrocortisol accumulates in cells cultured from trabecular meshwork specimens from patients with primary open-angle ***glaucoma***, but not in similar cells derived from nonglaucomatous patients. In view of the sensitivity of patients with primary open-angle ***glaucoma*** to the effects of glucocorticoids in raising intraocular pressure, this potentiation may be responsible for the steroid sensitivity and for the ocular hypertension seen in this disorder.

L6 ANSWER 36 OF 40 EMBASE COPYRIGHT
2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 82107525 EMBASE
DOCUMENT NUMBER: 1982107525
TITLE: Radioautography of dexamethasone in human eye tissues. A preliminary report.

AUTHOR: Tchermitchin A N.; Tchermitchin N., Anguita-Salas J., et al.

CORPORATE SOURCE: Dept Exp Morphol., Lab Exp. Endocrinol., J.J. Aguirre Hosp., Univ. Chile Med. Sch., Santiago, Chile

SOURCE: IRCS Medical Science, (1982) 10/3 (257)

CODEN: IRLCDZ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
030 Pharmacology
023 Nuclear Medicine
012 Ophthalmology

LANGUAGE: English
AB Glucocorticoid administration increases intraocular pressure in rabbits and humans. In the rabbit eye, radioautographic studies have localized ***glucocorticoid*** ***receptors*** in the aqueous production, suggesting their involvement in the pathogenesis of glucocorticoid-induced ***glaucoma***. Human eye tissue from 5 patients with open-angle ***glaucoma*** was obtained from trabeculectomy, incubated with tritiated dexamethasone, and submitted to the dry radioautographic

technique for diffusible compounds. Radioautograms revealed nuclear labeling in stromal and endothelial cells from the trabecular meshwork, scleral spur, the anterior face of ciliary body and iris root. The similarities between radioautographic findings in the rabbit and in the human eye suggests that the previously proposed hypothesis for the pathogenesis of glucocorticoid-induced increase in intraocular pressure in the rabbit may well be valid for the human eye.

L6 ANSWER 37 OF 40 WPIDS COPYRIGHT 2000
DERWENT INFORMATION LTD
ACCESSION NUMBER: 1981-83483D [45]
WPIDS

TITLE: Irreversible inhibition of glucocorticoid activity in subject - by admin. of cortisol or dexamethasone

21-mesylate(s)
DERWENT CLASS: B01
INVENTOR(S): SIMONS, S S
PATENT ASSIGNEE(S): (USGO) US
GOVERNMENT
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG
US 4296206 A 19811020 (198145)* 9

PRIORITY APPLN. INFO: US 1980-145350
19800430

AN 1981-83483D [45] WPIDS
AB US 4296206 A UPAB: 19930915

Inhibition of glucocorticoid action in a subject comprises admin. of cortisol 21-mesylate (I) or dexamethasone 21-mesylate (II).

Cpds. (I) and (II) are irreversible antiglucocorticoids; they have a low but significant cell-free affinity for the ***glucocorticoid***

receptors of rat hepatoma tissue culture cells and they inhibit tyrosine aminotransferase (TAT) induction in the cells. This inhibition of TAT is not due to cell toxicity. Cpds. (I) and (II) are the first known irreversible antiglucocorticoids, possibly because they form covalent receptor-steroid complexes.

Cpds. (I) and (II) may be used for blocking glucocorticoids in the treatment of non-operable hyperglucocorticoid syndromes esp. adrenal carcinomas and ectopic ACTH syndrome. Patients who can be treated are those hyper-responsive to glucocorticoids, e.g. with open-angle

glaucoma or those who are homozygous for the postulated gene defect causing this disease, with blocking some of the steroids and thus attenuating responses in sensitive cells. Cpds. (I) and (II) can also be used for pre-operative treatment of patients with Cushing's disease to eliminate the complications of surgery due to elevated glucocorticoid levels. They are also useful in studies of the mechanism of glucocorticoid hormone action, irreversible glucocorticoid activity is shown at 10 to minus 9 to 10 to minus 5 M.

L6 ANSWER 38 OF 40 EMBASE COPYRIGHT
2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 81237418 EMBASE
DOCUMENT NUMBER: 1981237418
TITLE: Autoradiography of 3H-dexamethasone following topical ophthalmic administration

AUTHOR: Tchermitchin N., Anguita-Salas J., Canas-Kramarsky M.M., et al.
CORPORATE SOURCE: Lab. Exp. Endocrinol., Dept. Exp. Morphol., J.J. Aguirre Hosp., Univ. Chile Med. Sch., Santiago, Chile
SOURCE: IRCS Medical Science, (1981) 9/9 (887-888).

CODEN: IRLCDZ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 012 Ophthalmology
023 Nuclear Medicine
037 Drug Literature Index
LANGUAGE: English
AB Previous results have shown ***glucocorticoid*** ***receptors*** in cells related to aqueous humor outflow, but not in cells related to its production, suggesting an explanation for the pathogenesis of glucocorticoid-induced ***glaucoma***. Ophthalmic glucocorticoids administered topically are widely used. This study describes local and systemic diffusion and localization of 3H-dexamethasone after topical ophthalmic administration in rabbits, using dry radioautography for diffusible compounds. Nuclear concentration of radioactivity is found in the same cell-types which have been proposed to be involved in the glaucomatous response; in addition, it was found in some extraocular target cells. This nuclear concentration of label is not observed in animals pretreated with excess of unlabeled dexamethasone, strongly suggesting competition and saturation of receptors. This study provides an explanation for the glaucomatous response that follows topical treatment with ophthalmic glucocorticoids, and alerts to the possibility of systemic dangerous effects.

L6 ANSWER 39 OF 40 MEDLINE
DUPLICATE 11
ACCESSION NUMBER: 82006886 MEDLINE
DOCUMENT NUMBER: 82006886
TITLE: Detection of ***glucocorticoid*** ***receptors***

in cultured human trabecular cells.
AUTHOR: Weinreb R N., Bloom E., Baxter J D., Alvarado J., Lan N., O'Donnell J., Polansky J R
CONTRACT NUMBER: EY02477 (NEI)
EY01785 (NEI)
EY02162 (NEI)

SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1981 Sep)

21 (3) 403-7.
Journal code: GWI ISSN: 0146-0404.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198201

AB To evaluate potential direct effects of glucocorticoids on the aqueous outflow pathway, the cellular binding of steroids to cultured human trabecular cells was examined. After incubation of cells with 5 to 40 nM [3H]dexamethasone, specific binding (i.e., binding that could be blocked by an excess of nonlabeled steroid) was detected by measuring the total cell-associated labeled hormone. A binding affinity of 5 nM and 60,000 receptor sites/cell were demonstrated with labeled dexamethasone. Incubation of human trabecular cells with 40 nM [3H]dexamethasone for 60 min revealed that 62% +/- 7 of the specific binding

was found in the
nuclear fraction and 38% +/- 3 was in the
cytoplasmic fraction. In
competition studies, dexamethasone had a higher
affinity for these sites
than cortisol, which in turn had a higher affinity than
progesterone.

These studies suggest that functional

glucocorticoid

receptors are present in human trabecular
cell cultures. Therefore

it is possible that a direct action of glucocorticoids on
trabecular cells

could contribute to the decreased outflow facility
observed in steroid

glaucoma

L6 ANSWER 40 OF 40 EMBASE COPYRIGHT
2000 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 78318236 EMBASE

DOCUMENT NUMBER: 1978318236

TITLE: ***Glucocorticoid***

receptors in primary

open-angle ***glaucoma***

AUTHOR: Palmberg P.; Becker B

CORPORATE SOURCE: Washington Univ. Sch

Med., St Louis, Mo., United States

SOURCE: Investigative Ophthalmology and

Visual Science, (1978)

17/Suppl. (208)

CODEN: IOVSDA

COUNTRY: United States

DOCUMENT TYPE: Journal

FILE SEGMENT: 037 Drug Literature Index

LANGUAGE: English